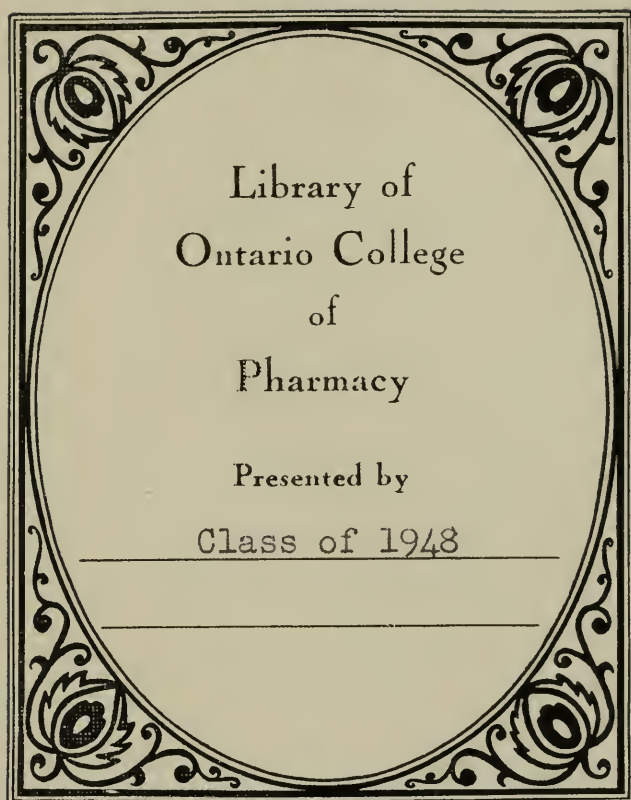




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ALLIED SCIENCES

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VOLUME 91

WITH INDEX, PREPARED BY E. FULLERTON COOK, PH.M.

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# THE AMERICAN JOURNAL OF PHARMACY

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JANUARY, 1919

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## EDITORIAL.

### SALUTATION.

The year that has just drawn to a close, has recorded on its historic pages some of the most momentous events that have ever occurred on this mundane sphere. It is too early yet to fully appreciate the enormity of the acts that have been crowded within the past twelve months and the after effects of these upon all the nations of the earth. Most heartily do all the thinking peoples look forward at this time to a long period of "Peace on Earth, Goodwill toward men." Pharmacy like every other human occupation has been in this turmoil and its practice may be materially altered by the evolutions of this war's melting pot.

As we stand at the threshold of another year, it is very appropriate to take a retrospective view of the work of the AMERICAN JOURNAL OF PHARMACY during the year that has elapsed since the editorial "Greeting" extended in January, 1918.

The editor believes that he has conscientiously endeavored to place before the readers such a varied "bill of fare" that the different tastes of the readers may have been satisfied. The wide scope of the articles published in the 90th Volume is shown by the Index, and despite the adverse trade conditions the volume exhibits an increase of about fifty per cent. of reading pages over former volumes.

We appreciate that this is due mainly to the support that has been so generously given by our contributors and patrons and to these we especially desire at this time to again extend our sincere thanks. It is our purpose to maintain throughout the new year and many years to come, by the grace of God and your support, the

Special Training gave us to understand that schools of pharmacy would receive the same treatment as is accorded to other institutions of learning, and that no special privileges would be extended to them as it was not within the province of the committee to grant special privileges. The published regulations on Student Army Training Corps fully cover the requirements demanded of any educational institution before they can secure the Student Army Training Corps unit. First: The institution must require for admission to its regular curriculum, graduation from a standard four year secondary school or its equivalent. Second: It must originally provide a general curriculum covering at least two years of not less than 32 weeks each. Third: It must have a student attendance sufficient to maintain a section of a Student Army Training Corps Unit of a strength of at least one hundred men. Colleges connected with universities that have an S. A. T. C. unit may secure these privileges even though they do not have one hundred students.

"Any college of pharmacy, as I understand it, that meets these requirements may have a Student Army Training Corps Unit.

"The committee made it clear that they do not consider it necessary that there be organized vocational units in colleges of pharmacy.

"The committee asked the men called in conference to prepare and submit to them a curriculum for colleges of pharmacy that in their opinion would meet the present war needs. The curriculum to be approved or disapproved by the Educational Committee, and if approved, to be used as a sample curriculum to be sent to all colleges of pharmacy that wish to maintain a Student Army Training Corps Unit.

"Very truly yours,

"C. B. JORDAN."

*Previous to the receipt of the above-mentioned wire from Washington on September 26, I had not attended nor been invited to attend any conference concerning this matter.*

When I received this wire, I assumed that the invitation came to me because I am President of the American Conference of Pharmaceutical Faculties, and so wired Dr. Koch asking whether the A. C. Ph. F. would pay my expenses to the meeting and stating the time and place of the meeting. While returning from the Washington Conference, I stopped in Pittsburgh, September 30, and had an interview with Dr. Koch in which I gave him a report of this conference.



Now, Mr. Editor, if I had anything to conceal, as is implied by your editorial, would I have notified Dr. Koch of the time and place of this meeting prior to the holding of the meeting or would I have stopped on my return trip and reported this meeting to him? If you wish confirmation of the above facts, address Dr. Koch.

From the above, it is plain that your accusations and implications of unfairness on our part are *false*.

It is a well-known fact that many of our larger and older colleges of Pharmacy do not require high school graduation or its equivalent for entrance and hence were not meeting the requirements of the War Department for the organization of Student Army Training Corps Units. Naturally, the Committee on Education and Special Training desired at this conference representatives of colleges of Pharmacy that *were* meeting their requirements. Yet they did have at this meeting representatives of colleges that are not connected with Universities and were not meeting the requirements, and, from the report in the *Journal* of the A. Ph. A., it is plain that at least one dean of a large and important proprietary college was invited to attend this meeting.

We are accused of unfairness because we were invited to attend this conference and some of the other colleges were not. In other words, we are unfair because our requirements meet those demanded by the War Department and we were ready to "deliver the goods" when the government needed them. This attitude seems to me to be the limit of "narrowmindedness."

When you wrote your editorial, did it occur to you that there were fifteen colleges of Pharmacy connected with Universities that were not notified of this meeting and were not invited to send delegates to it? If this were a deliberate attempt to favor those colleges connected with Universities, why were these fifteen institutions ignored? The Committee on Education and Special Training, evidently, had a definite work they wished accomplished and for this purpose it was not necessary or feasible to have representatives of all the colleges of Pharmacy called into this conference and hence they selected a few of each type of college to assist in preparing the program for Pharmacy Colleges.

You speak of "fractional spirit" in the conference. I can assure you that no one wishes to keep fractional spirit and discord out of the conference more than I do, and I regret exceedingly that you rushed into print before knowing the facts, because it is just such

rantings as are contained in your editorial that cause fractional spirit and discord.

Very truly yours,

C. B. JORDAN.

LINCOLN, NEBR., Dec. 28, 1918.

THE EDITOR OF THE AMERICAN JOURNAL OF PHARMACY,  
PHILADELPHIA, PA.

*My dear Sir:*—The November number of the AMERICAN JOURNAL OF PHARMACY contains an editorial concerning the War Department program with reference to the establishment of a pharmacy unit in the S. A. T. This editorial contains a number of errors and apparent misstatement of facts and as chairman of the Washington delegation, to which you refer, I feel that I should at least correct these errors, and upon you rests the responsibility of giving this statement the same publicity which you give the editorial in question.

There is no "history of that Sunday conference" which has not been made public. This was done through the natural channel—the *Journal* of the American Pharmaceutical Association. It was also printed in the *Northwestern Druggist*—whose editor asked for copy. After sending copy to Mr. Eberle, he suggested that I send copy to you. From your editorial I infer that you knew this. Knowing this, I felt that if you cared for copy you would ask for it personally. I do not see that I was under obligation to send it to you, without request, any more than I was to send it to any other pharmacy journal.

If you will read again the list of institutions asked to send representatives to the conference on September 29, you will see that your statement to the effect that this was a deliberate piece of politics on the part of the University schools, is untrue. Without mentioning names, a glance at that list shows that the Committee on Education and Special Training chose schools representing the various types of institutions constituting the American Conference. Why the Committee on Education and Special Training called the representatives they did, rather than any others, is not known to the representatives that met in Washington. It is probable, if you care for the information, that it might be obtained by addressing directly the chairman of the Committee on Education. I can only say that I believe that every man who was called to Washington



for that conference, did his work conscientiously, earnestly, and had only in mind the making of a program which would best carry out the idea the War Department had in mind in preparing men for the Service. The war is over and the S. A. T. C. is abandoned and we are permitted to return to our educational work on the pre-war basis. It seems to me that the fact that the War Department recognized the need of establishing a pharmacy unit in the S. A. T. C. in order to train men for army and civil life, is an act of considerable importance to the pharmaceutical profession. It can be viewed only as an advance step and is worthy of the widest publicity and favorable criticism. The attitude which you assumed in your editorial on this matter is most deplorable, chiefly because it makes one of the oldest and most respected of pharmaceutical journals smack of yellow journalism.

Very truly yours,

RUFUS A. LYMAN,  
*The University of Nebraska.*

The perturbation of our correspondents would make it seem that the editorial "A Quasi Recognition of Pharmacy" published in the November, 1918, issue of the AMERICAN JOURNAL OF PHARMACY served a useful purpose and that it had scored a direct hit.

The first of these communications, although bearing the date of December 11, was not mailed until December 26, and thus evidences ample time for reflection and consultation before promulgation. Although this correspondent had the personally written assurance of the editor that "my comment editorially had no reference whatever with your letter of the fourteenth of October and I had no reason whatever to take any exception to that communication. No one deprecates more thoroughly the introduction of 'factional spirit' in pharmaceutical circles than I do and my pointing out the danger of such was certainly not to be construed as an endeavor to encourage same," nevertheless, he insists upon its publication.

His ludicrous position is like that of one who persists in wearing a shoe that was not made for him and the size of which is so small that it will be a continuous discomfort to him and without the possibility of relief from the suffering.

What are the undeniable facts of the case? What is the unvarnished truth divested of the entanglement of high sounding phrases? When an individual or a group of individuals address a

communication "To the Pharmaceutical Profession of America" such a communication becomes public property and if meritorious is worthy of the widest dissemination. When an individual or a group of individuals announce that they "gave information concerning the colleges of pharmacy which would help the Committee on Special Training to determine the fitness of the various schools to become S. A. T. C. institutions," their judgment and the acts shown by their own statement become very rightly a subject for the consideration of pharmacists and it is well within the province of pharmaceutical journalism to discuss such an event and within the editorial prerogative to criticize the acts and decisions of such a self styled tribunal.

The editor lays no claim to infallibility of judgment nor is he willing to concede the claims of his correspondents to such. The pharmacists of this country are entitled to know the real facts and when the purport is understood their decision should determine the justness of our criticism.

The difference in positions is briefly this—the plan as contemplated would have limited the training of pharmacists for the government service to a few of the schools having membership in the American Conference of Pharmaceutical Faculties. The wisdom of the selection made, by which some of the most prominent and best equipped schools of pharmacy were deliberately ignored, was properly criticized. The selection was not only not the wisest that could have been made, but the discrimination manifested bias and was unfair and not sound advice either for the best interests of the nation or of pharmacy. Any scheme that discriminates between students of equal calibre, irrespective of whether their education was obtained in a university school or one not so affiliated, is an unamerican exhibition of cast.

Further the intended scheme would have debarred the thousands of pharmacists whose patriotism already had enrolled them in the Army, from the possibility of rendering the same service and receiving the same consideration as to ranking.

At the best, this scene was exactly as designated "A Quasi Recognition of Pharmacy" and not such an actual recognition of modern educated pharmacists as that accorded, by virtue of Congressional enactments, to the other divisions of medicine represented in the Army Medical Department, and certainly not comparable with

the fair recognition of pharmacy for which representative pharmacists have been contending in their plea for a pharmaceutical corps.

The editor is contending for a proper and adequate recognition of pharmacy. A recognition that shall not be based upon arbitrary discriminations and an assumption of superiority that exists in the assumption only and for a pharmaceutical corps that shall be open to all properly equipped pharmacists and that will provide for and protect the interests of the pharmacists who are already in the Army service.

Which plan is loyal to the best interests of pharmacy? In which is the yellow streak? Is it in the latter perfectly fair proposition or is it in a scheme that contemplated the dumping of the Edmonds Bill and the principles advocated by pharmacists as the basis for the establishment of a pharmaceutical corps in the U. S. Army?

It is not the purpose of the editor to engage in controversies nor does he intend to prolong the present difference of opinion. He believes that he performed his duty in directing attention to the attempt to divert what might have been made a great movement to the general benefit of pharmacy and its appropriate recognition to the selfish advantage of a few and has no apologies to offer. He has his own opinions regarding the entire matter at issue and more recent information but tends to support his views. He has no objection to his fellow pharmacists holding views of their own or of seeking their self advancement by ethical methods along truly *professional and scientific avenues*. He is now quite willing to rest this case with the American Pharmacists as the jury.

In conclusion he suggests that future communications from these correspondents be of constructive value to pharmacy. The AMERICAN JOURNAL OF PHARMACY will welcome from them communications of this character as coming more within the scope and policy of this JOURNAL.

GEORGE M. BERINGER.

### THE CREED OF HAPPINESS.

Get up right in the morning. Go to bed right at night. Start with joy in your heart, hope in the future, kindness in your purpose.

If it is a dark day, never mind; you will brighten it up. If it is a bright day, you will add to the brightness. Give a word of cheer, a kindly greeting and a warm handshake to your friends.



If you have enemies, look up, pass them by, forget and try to forgive.

If all of us would only think how much of human happiness is made by ourselves, there would be less of human misery.

If all of us would bear in mind that happiness is from within and not from without, there would be a well-spring of joy in every heart and the sun would shine forever.—*Leslie's*.

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## ASSOCIATION MEMBERSHIP—A WISH FOR 1919.

BY E. G. EBERLE, PH.M.

The relation between the American Pharmaceutical Association and the American Medical Association should be such that members of the latter place utmost confidence in these of the former, and reversely. This creates public confidence in the individuals, in the practice of medicine and of pharmacy.

The American Pharmaceutical Association should be so generally and so favorably known that it gives the members a standing in the community as peers of their profession. The same thoughts apply relatively to state associations. As a matter of fact the people do take cognizance of whether a pharmacist is an active association member or not. Every progressive individual associates himself with others in his trade or profession, hence such conclusions are rational. We judge others from our own viewpoints. Membership in an association marks the member as one who is associated with the best men in his profession, engaged in efforts to raise the standard of his calling; and makes it more deserving of public confidence. He becomes known as one of a large number in his profession who stand for the best service—service to the profession and for the welfare and better health of the human race. Membership in associations sharpens the wits of the members, for they come in contact with the foremost men of the profession. It gives the members a higher appreciation of their profession and also of those likewise engaged—an inspiration to promote pharmacy and contend for its rightful recognition. We have both individual and collective responsibilities,—now, as never before, should the spirit of the Golden Rule be generally applied.

The progress of pharmacy depends upon a deeper, more intense,

interest of the individuals in each other, and coöperation in associated work. Chemists and medical men have determined that their associations will grow and that their professions will make forward strides; let us hope that pharmacists have the same intentions.

In the *Journal* of the American Pharmaceutical Association for December, 1918, I have expressed this wish:

That pharmacy may progress during 1919 through a greater enthusiasm and better coöperation among the members of the Association; a willingness to make some personal sacrifices so that pharmacy and the Association may become more affective as an agency for good to the votaries, and of greater service to humanity. That there may come the realization that however much pharmasists may have done for pharmacy and the Association, they, themselves, have profited more, by giving. That pharmacists and druggists may develop a larger measure of professional and business efficiency, upon which the world is now putting so large a premium. That the year 1919 will be the biggest year in the world's history for pharmacy and the drug business, because the achievements, successes and progress of the past are added to its opportunities.

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## THE INFLUENCE OF THE PRESENCE OF STEMS AND ROOTS UPON THE TOTAL ALKALOID CONTENT OF THE LEAVES OF STRAMONIUM.

BY GEORGE P. KOCH, PH.D.

Can the stems of stramonium be used with the leaves for commercial purposes? In dealing with stramonium, this question is of no small importance at the present time. The relative importance attached to the possibilities of the use of stramonium stems is not due to the scarcity of the leaves of stramonium, but to the cost of labor in harvesting. The question easily resolves itself into the fact, that if the stems could be utilized the cost of labor in harvesting a crop of stramonium would be about one fourth to one fifth of the cost in harvesting where the leaves alone are considered, since perfected machinery could readily be employed.

This factor of the utilization of stems in conjunction with the leaves in the case of belladonna and hyoscyamus will also be considered in later publications.

The U. S. Pharmacopeia requirement for stramonium leaves, calls for leaves without the presence or admixture of more than 10 per cent. of stems or other foreign material, and yielding 0.25 per cent. of the total alkaloids of stramonium.

In searching through the available literature it seems evident that this factor of utilizing stems has not been given very much consideration.

To secure more information on the possibilities and advisabilities of employing stems and roots of stramonium in conjunction with the leaves, a series of experiments covering this phase were made.

Fifteen representative plants of stramonium were taken from the field, being very careful to retain all the leaves and roots. These plants were brought to the laboratory, and the leaves, secondary stems, primary stems, and roots were carefully separated from each plant, and placed in manila paper bags and dried at a temperature of 50° to 60° C. The leaves represented not only the entire leaf, but included the flowers and seed pods where present. The primary stems included the woody portion; the secondary stems included the smaller portions of stems; the roots included all the root which was cut from the base of the stem.

Since the stramonium plants are exceedingly pulpy it was thought quite necessary to determine the percentage of moisture in each part of the plant. Hence moisture determinations were made of the various parts of four plants and the data is recorded below.

TABLE I.

TABLE SHOWING THE MOISTURE CONTENT OF THE VARIOUS PARTS OF STRAMONIUM.

Plant No.	Leaves, Per Cent.	Secondary Stems, Per Cent.	Primary Stems, Per Cent.	Roots, Per Cent.
1	81.4	88.5	85.8	81.5
2	82.0	91.9	86.8	78.2
3	81.9	90.4	85.0	79.1
4	84.6	91.3	85.8	79.0

The results presented above show that the stramonium plants contain a high percentage of moisture, *i. e.*, leaves averaging 81 to 85, stems 85 to 92, and roots 78 to 81 per cent.

The samples of stramonium which were submitted for analysis for total alkaloid content were made up as follows: The dry leaves



of each of five plants were carefully mixed together. Hence, since fifteen plants were collected, there resulted three large samples of leaves. Similarly the secondary stems of the same five plants were mixed, thus resulting in three samples of secondary stems. The primary stems and roots were, in like manner, mixed.

In making these samples, great care was taken so as to have small, medium, and large plants in each group of five plants. Hence each sample represented as good an average of plants as could be expected under field conditions. Thus the samples which were submitted for analysis were as follows: Three samples each of leaves, secondary stems, primary stems and roots. Since the U. S. P. calls for leaves of stramonium with the addition of not more than 10 per cent. of foreign material, it was thought desirable to prepare samples containing the largest amount of inert matter that the U. S. P. would permit, and so three samples of leaves with the addition of 10 per cent. secondary stems were also submitted for analysis. If machinery is to be employed in harvesting stramonium, the leaves, the secondary and the primary stems would all be contained in the product, as the plants would be cut off near the ground. Consequently to determine to what extent the added stems reduce the total per cent. of alkaloid, samples were prepared in which the leaves and stems were in the same proportions, by weight, as when they grew in the field. Similarly samples in which leaves, stems and roots were considered in their proportion under growing conditions, were prepared.

To show in what relation the leaves are to the stems on the plants in the field, a table of data is presented.

TABLE II.

TABLE SHOWING THE RELATION OF THE LEAF TO THAT OF STEMS OF STRAMONIUM.

Sample No.	Leaves, Per Cent.	Secondary Stems, Per Cent.	Primary Stems, Per Cent.
211	48.3	24.7	27.0
212	46.5	26.0	27.5
213	47.3	23.6	29.1

The results show that with these fifteen plants under consideration, the proportion of leaf is slightly smaller than that of all the stems.

The following table is inserted to show the relation in which the roots, stems and leaves appeared in the fifteen plants here under consideration.

TABLE III.

TABLE SHOWING THE RELATION OF LEAF TO THAT OF STEMS AND ROOTS OF STRAMONIUM.

Sample No.	Leaves, Per Cent.	Secondary Stems, Per Cent.	Primary Stems, Per Cent.	Roots, Per Cent.
211	41.4	21.3	23	14.4
212	40.8	22.8	24	12.3
213	39.1	19.5	24	17.3

As presented above in Table III, where the root is also considered a part of the whole, the leaf represents about 40 per cent. of the total portion of the plant.

The samples of stramonium as presented for analysis consisted of from 40 to 100 gms. of material in each sample, and in every case the entire amount was carefully ground. From this ground material the sample for the determination was taken.

TABLE IV.

TABLE SHOWING THE ALKALOID CONTENT OF THE VARIOUS PARTS OF THE STRAMONIUM PLANTS, AND THE RESULTS PRODUCED WHEN VARIOUS PERCENTAGES OF STEM AND ROOTS WERE ADDED TO THE LEAVES.

Sample No.	Kind of Material.	Mydratic Alkaloid.
211	Leaves.	0.539
212		0.596
213		0.398
214	Secondary stems.	0.660
215		0.634
216		0.404
217	Primary stems.	0.080
218		0.127
219		0.160
220	Roots.	0.215
221		0.319
222		0.377
223	Leaves + 10 per cent. stems.	0.385
224		0.473
225		0.513
226	Stems + leaves in their proportion.	0.225
227		0.483
228		0.393
229	Leaves, stems, roots proportionately.	0.352
230		0.431
231		0.557



The results as presented above show conclusively that the total alkaloid content of both the leaves and secondary stems run very high, in most cases more than twice the U. S. P. requirement. Hence there should not be a question with regard to the use of the secondary stems in conjunction with the leaves, as the alkaloidal requirement of the U. S. P. could be very easily met. The alkaloid content of the primary stems is considerably lower than that of the secondary stems. In all cases these figures were considerably below 0.25 per cent. or the minimum requirement. This is not the case with the roots, however. In samples Nos. 223, 224 and 225, in which the admixture of just 10 per cent. of stems was employed, a very high alkaloid content was realized. In one case 0.51 per cent., or twice the U. S. P. requirement, was appreciated. The most important data to be considered is that from Nos. 226, 227 and 228, in which cases the leaves and stems, as they would exist in the field, as if harvested by a mowing machine and the whole plant utilized, are presented. In two cases the percentage of alkaloid content went far above the U. S. P., while in the third case it was only 0.025 per cent. below that requirement. Hence there hardly seems a question but that on the whole if leaves and stems were both employed, and they were utilized in the proportion in which they existed in the field, the U. S. P. requirement, with regard to the alkaloidal content, would always be met. The same might be said with regard to stramonium material where leaves, stems and roots are utilized since in all determinations, the total alkaloid content was far above the requirement.

In so far as the material at hand will permit, the data set forth in these experiments lead to the following conclusions:

1. The moisture content of the various portions of stramonium plants are as follows: Leaves 80 to 85 per cent., secondary stems 87 to 92 per cent., primary stems 85 to 87 per cent., and roots 78 to 82 per cent.

2. When the whole plant, not including the root, is considered, the ratio of the leaf to the whole stem is about 47.5 to 52.5.

3. In considering the leaf, stem and root, the leaf represented about 41 per cent. of the whole.

4. The total mydriatic alkaloids, of the leaf and secondary stems when analyzed individually or the leaves with 10 per cent. of the secondary stems, run much higher than the U. S. P. requirement.

5. The whole plant either with or without the root can be har-

vested and used for the commercial preparation without fear of the total alkaloid content falling below 0.25 per cent., which is the desired standard.

I am indebted to Mr. George E'Ve and the analytical department for having made all of the alkaloid determinations and I wish to take this opportunity to express my thanks in this connection.

BIOLOGICAL LABORATORIES,  
H. K. Mulford Co.,  
GLENOLDEN, PA.

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## THE EARLY HISTORY OF PERCOLATION.

BY JAMES F. COUCH.

The use of a process analogous to percolation for the extraction of soluble matters from their admixture with an insoluble residuum has been traced back to the ancient Greeks, centuries before our era, by Raubenheimer.<sup>1</sup> The application of the process to pharmacy, however, dates from much more recent times. In fact, the exact date of its introduction as well as the pharmacist to whom belongs the honor of establishing the method for the extraction of drugs is still within the realm of controversy. Conflicting claims have been advanced by various writers and no one has, as yet, devoted the time necessary to make a serious study of this question, to weigh the published evidence, and to offer a conclusion.

I have, during the past four years, been collecting data on percolation, for other purposes than the strictly historical, and in the course of this work have been able to review the early literature and obtain sufficient material to cast much light upon the origin of percolation in pharmacy. It seemed of interest to present this material and the conclusions to be drawn from it to American pharmacists since they have done more to develop and apply the process of percolation than any others.

It is certain that percolation was unknown as a pharmaceutical process as late as the beginning of the eighteenth century for the curious "*Pharmacopée Universelle*" of Doctor Nicholas Lemery, which was published in 1698, does not mention it. Lemery, however, gives detailed and complete directions for carrying out all sorts

<sup>1</sup> This JOURNAL. vol. 82, p. 32, 1910.

of pharmaceutical operations; none of these even remotely resembles percolation, and his work is so exhaustive that he could hardly have overlooked it had it been in common use at that time. His directions for preparing extracts were maceration with subsequent pressing out of the marc.

The earliest recorded forms of apparatus in which percolation might be carried out are a sort of percolator used by the sugar refiners in decolorizing their syrups and the cafetière of Dubelloy, both in common use early in the nineteenth century and mentioned by the Boullays.

It was probably from the cafetière of Dubelloy that Benjamin Thompson, Count of Rumford—born at Woburn, Mass.—obtained the ideas which led to his improved processes for the preparation of coffee<sup>2</sup> in which he utilized an apparatus very much like a percolator. Rumford himself states that he did not know who first proposed the method. In his own words, his process was:

“Now when coffee is made in the most advantageous manner, the ground coffee is pressed down in a cylindrical vessel, which has a bottom pierced with many small holes so as to form a strainer; and a proper quantity of boiling water being poured cautiously on this layer of coffee in powder, the water penetrates it by degrees, and after a certain time begins to filter through it. This gradual percolation brings continually a succession of fresh particles of pure water into contact with the ground coffee, and when the last portion of water has passed through it, everything capable of being dissolved by the water will be found to be so completely washed out of it, that what remains will be of no kind of value.”

It will be noted that Rumford uses the term “percolation,” possibly the first use of it in this connection. We next find it in Duhammel’s memoir<sup>3</sup> on the process of displacement. Rumford’s device is more properly an apparatus for the preparation of infusions than a percolator and, except for historical interest, has no connection with the percolation of pharmacy.

The “filter press” invented by Count Réal<sup>4</sup> and described by C. L. Cadet, was an hexagonal box of tin to the top of which was fitted a vertical pipe or column, six to eleven feet in height, to exert,

<sup>2</sup> Repertory of Arts, Manufactures, and Agriculture, 2d series, vol. 22, pp. 274, 339, 1813.

<sup>3</sup> This JOURNAL, vol. 10, p. 1, 1838.

<sup>4</sup> *Jour. de Pharm.*, vol. 2, pp. 165, 468, 1816.



when filled with water, hydrostatic pressure upon the contents of the "press." For such occasions where more pressure was required than would be furnished by the column, Réal contrived a shorter column of mercury arranged to exert its pressure indirectly upon the press. Cadet thus describes the operation of the press:

"Une poudre végétal, equisée de principes solubles et détemperée avec de l'alcool rectifié, est mise dans l'appareil; on fait agir dessus la colonne d'eau. Cette eau ne se mêle point avec l'alcool; celui-ci passe au même degré aréométrique qu'il avait avant l'expérience.

"Le filtre-presse me parut donc infiniment utile et même indispensable pour préparer les extraits des plantes dont les principes immédiate sont altérés par la caloric."

The drug was moistened and allowed to swell before being placed in the apparatus. Cadet reports good results in using this method with cinchona, belladonna, aconite, and conium. The method was not in any sense a process of percolation; the drug was not exhausted by the addition of successive quantities of menstruum but was handled exactly as in the old process of maceration with the exception that the marc was freed from adhering tincture through displacement instead of by pressing out in a tincture press. Cadet, far from realizing the possibilities which lay in the apparatus, preferred the older process, saying of Réal's press:—"la manipulation est longue, compliquée, minutieuse."

During the following year Johnson<sup>5</sup> described the preparation of an infusion of cinchona, for which he used an apparatus and process no different from that described by Rumford, and similar to one which, he says, was made by Edmund Loyd & Co. "several years ago."

In 1825 Donovan<sup>6</sup> described an apparatus for filtering caustic soda out of contact with the atmosphere. Although he did not apply it to the extraction of drugs it is, in fact, an anticipation of many forms of percolators designed to prevent loss of volatile menstrua. The percolator is fitted tightly into a receiver furnished with a side neck from which a tube extends upward and is bent to fit into the top of the percolator through a stopper. Army<sup>7</sup> and others have suggested similar arrangements.

<sup>5</sup> Thompson's *Annals of Philosophy*, vol. 9, p. 451, 1817.

<sup>6</sup> *Annals of Philosophy*, August, 1825, *Jour. de Pharm.*, vol. 11, p. 519, 1825.

<sup>7</sup> *Proc. Am. Ph. A.*, vol. 40, p. 169, 1892.

MM. Boutron and Robiquet<sup>8</sup> during a chemical investigation of mustard seeds discovered a case of true displacement which they report as follows:

" . . . we took the flour of white mustard from which the greater part of the fixed oil had been extracted by pressure and we introduced it into a large and long tube constricted at one end and closed by a glass stopper at the other. This tube was filled with ether and closed immediately. This tube was adjusted so that the ether could flow only very slowly. This menstruum acted upon the oil with a sort of repulsive force, it chased it, so to speak, before it, in such a way that that which first flowed out was the oil nearly pure and which scarcely smelled of ether."

Robiquet later (1834)<sup>9</sup> claimed to have observed the same phenomenon while investigating the oil of bitter almonds. His original memoir was read<sup>10</sup> before the Académie des Sciences and an abstract of it published in the *Journal de Pharmacie*. This abstract does not mention the displacement. A thorough search of contemporary journals failed to reveal any trace of the original memoir in its entirety.

On May 2, 1833, the first of the classical papers of MM. Boullay, père et fils, was read before the Société de Pharmacie.<sup>11</sup> It is noteworthy that the Boullays give full credit to Dubelloy, Real, and MM. Boutron and Robiquet for their prior work. After showing the uselessness and inconvenience of the column of Real they insist upon the importance of the principle of displacement:

"Lorsqu'une poudre saturée d'eau, mais incapable de former pâte avec elle, est placée dans un récipient analogue à celui du filtre-pressé de M. Réal, si l'on fait agir sur elle le colonne d'eau, cette eau traverse la poudre en chassant complètement devant elle le liquide qui la mouille, et la remplace sans s'y mêler."

Further investigation resulted in a second memoir<sup>12</sup> in which they especially considered the pharmacy of cinchona. The drug, in fine powder, was moistened, allowed to swell, packed and percolated with water. The percolate was collected in five fractions,—volume not stated,—and the weight of dry extract from each re-

<sup>8</sup> *Jour. de Pharm.*, vol. 17, p. 279, 1831.

<sup>9</sup> *Jour. de Pharm.*, vol. 20, p. 79, 1834.

<sup>10</sup> *Ibid.*, vol. 17, p. 144, 1831.

<sup>11</sup> *Jour. de Pharm.*, vol. 19, p. 281, 1833.

<sup>12</sup> *Jour. de Pharm.*, vol. 19, p. 393, 1833.

ported. As a sign of their carefulness and observation it may be remarked that they noticed a sensible difference in the extracts yielded by these different fractions! This is highly interesting in view of the later work of Squibb.<sup>13</sup> The Boullays recognized the fact that the residual liquor in the marc left by the old process is of the same composition as that pressed out. They again insist upon the importance of the principle of displacement and name the process the "method of displacement."

"Que le déplacement immédiat et continu, appliqué à de faibles quantités de liqueurs, devra être généralement adopté dans ce genre d'operations; car les premiers produits sont excessivement concentrés, et la force de ceux qui suivent décroît dans une proportion extrêmement rapide."

Pelouse<sup>14</sup> used percolation in his work on nut galls; "Le tannin extrait de la noix de galle par l'éther hydraté à l'aide de la méthode de déplacement est incolore et sans odeur, etc." He gives no credit for developing the process.

During the next year Robiquet<sup>15</sup> inserted in his account of meconic acid a description of his percolator:

"Je profiterai de l'occasion pour faire connaître plus généralement l'appareil dont je me sers depuis plusieurs années, et dont il a déjà été fait mention dans le mémoire que j'ai publié conjointment avec M. Boutron, sur l'huile d'amandes amères."

This is the same apparatus described in 1831. Robiquet had taken no notice of the work of the Boullays up to this time.

Another memoir by the Boullays appeared in 1835.<sup>16</sup> In this they extend the process to new drugs and quote the results obtained by several pharmacists in the use of displacement. They now assert priority over Robiquet, resenting the statement of Guibourt<sup>17</sup> who had given their apparatus the name of the "displacement funnel of Robiquet," and those of Bonastre<sup>18</sup> who stated:

"J'ai essayé de mettre en usage le procédé de déplacement indiqué par nos honorables collègues Robiquet et Boutron Charlard, et en dernier lieu par M. Boullay."

<sup>13</sup> This JOURNAL, vol. 39, p. 402, 1867.

<sup>14</sup> *Annales de Chimie et de Physique*, December, 1833; *Jour. de Pharm.*, vol. 20, p. 356, 1834.

<sup>15</sup> *Jour. de Pharm.*, vol. 20, p. 79, 1834.

<sup>16</sup> *Jour. de Pharm.*, vol. 21, p. 1, 1835.

<sup>17</sup> "Traité de Pharmacie," Tome II, p. 39.

<sup>18</sup> *Jour. de Pharm.*, vol. 20, p. 281, 1834.



This memoir is illustrated with a cut of the Boullays percolator, the distinctive features of which are the conical shaped bottom and the two perforated diaphragms on one of which the drug is to rest while the second is used to prevent disturbance of the surface of the drug on the addition of menstruum. The Boullays refer to the fact that many pharmacists had already used the apparatus of the sugar refiners and also attended to the remarks of Geiger (see below).

Robiquet<sup>19</sup> now took notice of the Boullays' work being urged to do so, as he says, by his friends. He now, for the first time, makes some pharmaceutical application of the process. His paper is a curious document for he appears to attach no importance to the honor for which he contends. Indeed, he speaks almost contemptuously of the process, viz., "I have never attributed the least importance to an affair which offers, after all, only a puny application of the filter of Real." He abandons to the Boullays all the priority for their apparatus, although he claims to have used the process for ether extractions during ten years and asserts that he had had his apparatus made in glass by M. Aloque who carried it in stock afterward and that many pharmacists had asked for it under the name of the "apparatus of Robiquet."

The reply of P. F. G. Boullay to this paper was immediate and satisfactory.<sup>20</sup> Boullay makes no pretension to any discovery of any apparatus for percolation, though he had an obvious right to do so, but claims to have newly applied the principle of washing by means of displacement to a number of drugs and to have demonstrated the uselessness of the column of Real. He insists, significantly, upon the "inevitable revolution which pharmacology will undergo through the general application of the method of displacement," a prophecy which has been amply fulfilled.

The thesis of M. A. Guillermond<sup>21</sup> "De l'emploi de la méthode de déplacement dans les préparations pharmaceutiques," sustained at the School of Pharmacy of Paris presented a very complete examination of the process of displacement, comparing it with maceration to the disadvantage of the latter process. Guillermond gives to Robiquet and Boutron the credit for having introduced the process to organic chemistry, but gives the honor of extending its applica-

<sup>19</sup> *Jour. de Pharm.*, vol. 21, p. 113, 1835.

<sup>20</sup> *Jour. de Pharm.*, vol. 21, p. 188, 1835.

<sup>21</sup> *Jour. de Pharm.*, vol. 21, p. 349, 1835; this JOURNAL, vol. 10, p. 308, 1836.

tions to pharmacy and demonstrating its usefulness there to the Boullays. This evidence of contemporary opinion is important, particularly as it is voiced by a man who had made an extensive investigation of the whole problem. Guillermond also confirms the Boullays conclusion of the uselessness of the column of Real. It is interesting to note that all of the many new forms of percolating apparatus which utilize this method for exerting pressure on the contents of the percolator have been uniformly rejected by pharmacists.

When Guillermond's thesis was reprinted in the *Annalen der Pharmacie* (without the acknowledgments which literary courtesy demands) Geiger<sup>22</sup> appended to it a critical commentary in which he exhibits much mental confusion, being unable to distinguish the totally different nature of the principles involved in the processes of Real and Boullay; in addition,—we are almost led to say with racial characteristic,—he claims that the knowledge of the process was already widespread in Germany and adds, “and, apparently, in France.” Of these statements he offers no proof whatsoever, and, however well the process may have been thought to have been known in Germany before the Boullays published their investigations, an examination of the literature will show that such knowledge was derived wholly from French sources and none of it was original. What may have been done outside of the literature we have no means, at this date, of knowing. A consideration of what the Germans have done with percolation since that time will, however, leave any American, who is familiar with the detailed and extensive investigations of American pharmacists, very much in doubt as to whether the Germans have ever thoroughly understood the principles which underlie percolation or not. In this connection a paper by Vielguth and Nentwich,<sup>23</sup> “On the most correct methods for preparing extracts,” may be consulted.

The new process must have attracted widespread attention in France. Dausse, ainé, invented a percolating apparatus to which he added a water bath and still.<sup>24</sup> Dausse investigated the extraction of eighty drugs, a labor of no small moment.

<sup>22</sup> *Annalen der Pharmacie*, vol. 15, p. 95, 1835.

<sup>23</sup> Wittstein's *Vierteljahresschrift*, y. 1858, pp. 321, 481; this JOURNAL, vol. 31, p. 233, 1859.

<sup>24</sup> Abs. in *Jour. de Pharm.*, vol. 21, p. 369, 1835.



Soubeiran,<sup>25</sup> in 1836, published the results of his researches on the method of displacement, having experimented on sixty drugs. He considered the apparatus of the Boullays the best. Although, like Guillermond and others, he accepts Vauquelin's experiment of washing brine out of sand with fresh water as a proof of displacement, he shows that water will not displace alcohol from a drug without mixing with it, in this controverting the Boullays. As to the question of priority he has this to say:

"Lixiviation was not applied to pharmaceutic preparations, or rather this application was almost forgotten when MM. Boullay pointed out the advantages of it. . . . It is true M. Payen had advised this process, and M. Robiquet had employed it in certain chemical investigations, but its real application to pharmaceutic preparations appears to be owing to MM. Boullay."

The memoirs of Guillermond and Soubeiran were published in this JOURNAL soon after their appearance in the French periodicals. Elias Durand of Philadelphia immediately adopted the process and was probably the first American pharmacist to employ it. Augustine Duhammel, in 1838, wrote the first American memoir on the process and from that time on, American pharmacists have led the world in studying and applying percolation.

This, then, is the evidence upon which we must base our conclusions as to whom is due the honor of being the "Father of Percolation." Dubelloy and Count Rumford may be eliminated for, although their processes were very similar to percolation, they were intended only for the preparation of an infusion of coffee as a beverage and were not extended to pharmacy at all. The process of the sugar refiners may be disregarded for it was not an extraction process as we understand percolation: the solution was percolated through a decolorizing mixture to which it yielded a substance rather than that a solvent was passed through a mixture from which it dissolved soluble material. Real's filter press method, again, was not percolation: it attempted no exhaustion of the drug but merely to substitute a displacement for the previously used tincture press. Real's principle was, thus, entirely different from those which govern percolation.

Had Johnson continued his work there is no doubt that he would have discovered the process of percolation. As it was, he stopped

<sup>25</sup> *Bul. Gen. de Therapie*; this JOURNAL, vol. 10, p. 221, 1836.

with the method for preparing an infusion of cinchona and did not even attempt to use it for preparing other infusions or extracts.

Robiquet and Boutron undoubtedly were the first to extract drugs by a process which is identical with our present percolation. They packed their material in a true percolator and exhausted it with successive portions of solvent. Ether was the solvent usually employed by them, but Robiquet stated that alcohol or water might also be used where desirable. The percolating apparatus of Robiquet was used by several Parisian pharmacists who, therefore, appreciated the value of the new method of extraction.

Robiquet and Boutron, however, made no application of this new process to the extraction of drugs for pharmaceutical purposes and it was not until two years after the publication of the first memoir of the Boullays that Robiquet did offer a description of its use in pharmacy. Indeed, Robiquet was unable to conceive the possibilities of the process and, as his above quoted remarks amply show, considered percolation a trifling affair quite unworthy of much thought or effort.

The work of the Boullays, on the contrary, was devoted to the establishment of percolation as the method of extracting drugs. They compared it with the old process of maceration and demonstrated its superiority, which Cadet, using the Real apparatus, was unable to do. They showed the uselessness of the long column which Real contrived to obtain pressure. But the most noteworthy feature of the Boullay memoirs is their insistence upon the great future of the method of displacement, as they termed it, and of the revolution in pharmaceutical practise which it must bring about.

The Boullays exhibited a pharmaceutical skill and knowledge which neither Robiquet nor Boutron showed. Indeed, the latter were more nearly pure chemists, as was Vauquelin, than pharmacists.

Lastly we have the contemporary opinions of Guillermond, Soubeiran and Duhammel, who all accord to the Boullays the honor of applying percolation to pharmacy.

I have no desire to depreciate, in the slightest degree, the credit which belongs to MM. Boutron and Robiquet for having introduced percolation into organic chemistry: their work is analogous to that of Soxhlet and does no more pertain to pharmacy than his; but I think the evidence leads clearly to a single conclusion and that is that to the Boullays, father and son, belongs the honor of establishing the process of percolation in the art of pharmacy.

### SUMMARY.

1. MM. Boullay, père et fils, should be accorded the credit for establishing percolation as a pharmaceutical process.

2. To MM. Boutron and Robiquet belongs the credit for introducing percolation into the methods of organic chemistry.

3. Guillermond, Soubeiran and Dausse deserve special credit for their careful investigations of percolation which did much to further the establishment of the process in pharmacy.

4. There is no reliable evidence to show that German apothecaries were acquainted with the principles of percolation before the publication of the investigations of French pharmacists.

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### PLANTS USED AS INSECTICIDES.<sup>1</sup>

BY R. C. ROARK.

In the course of investigations on the use of insect powder and hellebore as insecticides, the author has noted many references in the literature to the insecticidal action of other plants. In view of the desirability of finding new insecticides, especially at the present time when the price of arsenicals, pyrethrum (insect powder) and many other insecticides is so high, it has seemed desirable to compile these statements and to bring them to the attention of entomologists, pharmacists and others.

Tons of the rhizome and rootlets of *Veratrum viride* Ait. are used annually in preparing hellebore, and during the fiscal year 1916-17, insect flowers (*Chrysanthemum cinerariæfolium* Benth. & Hook.), which, when finely ground, form insect powder, were imported into this country to the value of over \$300,000. In addition, large amounts of larkspur, sabadilla, quassia, red cedar shavings and tobacco dust are consumed in the preparation of insecticides. It is thus seen that there is a large market for plants as insecticides, and that but a very few species are at present utilized in this manner.

In view of the large number of plants possessing poisonous properties, it seems surprising that so few are used commercially as insecticides. Probably the majority of the plants here listed have no

<sup>1</sup> Contribution from the Insecticide and Fungicide Laboratory, Miscellaneous Division, Bureau of Chemistry, Department of Agriculture, Washington, D. C.



commercial value at present, and many are troublesome or even dangerous weeds. If these could be utilized for insecticidal purposes a market would be found for material that is at present valueless or even the cause of direct loss, *e. g.*, from stock poisoning.

It is believed that some of the plants listed may be found to be of commercial value as insecticides.

These references have been collected from many sources, but most of them are taken from the following works:

Greshoff, M., "Mededeelingen mit 'S Lands Plantentuin XXIX" *Tweede gedeelte van de Beschrijving der Giftige en bedwelmende planten bij de Vischvangst in begruik.*" Batavia, 1900.

Greshoff, M., "Mededeelingen uitgaande van het Department van Landbouw No. 17, Derde gedeelte (Supplement) von de Beschrijving der giftige en bedwelmende planten bij de vischvangst in gebruik." Batavia, 1913.

Kalbruner, Hermann, "Ueber die Insektenvertilgende Wirkung einiger Pyrethrumarten," *Zeitschrift des allgemeinen oesterreichischen Apothekervereines*, vol. 12, no. 29, October 10, 1874, pp. 542-543.

Lyons, A. B., "Plant Names, Scientific and Popular," 2d ed., Detroit, 1907.

von Mueller, Baron, Ferd, "Select Extra-Tropical Plants," 9th ed., Melbourne, 1895.

Pammel, L. H., "A Manual of Poisonous Plants," Part I, 1910; Part II, 1911, Cedar Rapids, Iowa.

Porcher, Francis Peyre, "Resources of the Southern Fields and Forests," rev. ed., Charleston, 1869.

Riley, C. V., Fourth Report of the U. S. Entomological Commission, Washington, 1885.

In the case of statements obtained from other sources, the full reference is given immediately following the statement.

This list is presented as a preliminary one only, but it seemed advisable to publish it at the present time in order that tests on the insecticidal properties of the plants might not be delayed.

It is realized that the synonymy and classification of the species as to family will not satisfy all botanists. Furthermore, in many cases an author gives both the common name and the scientific name of a plant, which do not agree. For example Riley speaks of *Helenium autumnale* and *H. tenuifolium* as dogfennel, whereas dogfennel is *Anthemis Cotula* L. In such cases the scientific name

given has been retained, and the common name changed. In preparing this list the object has been to name the plant so that it could be identified, rather than to prepare a list of synonyms or a botanical classification.

The author will greatly appreciate any information in regard to additional plants reputed to have insecticidal<sup>2</sup> action and also in regard to tests upon insects made with any plants, whether listed here or not.

The author wishes to acknowledge his indebtedness to Mr. G. L. Keenan, of the Micro-chemical Laboratory, Bureau of Chemistry, who has very kindly aided in classifying the plants as to family<sup>3</sup> and in correcting typographical errors.

ACHILLEA NOBILIS L. *Compositæ*. Noble Yarrow. Central and Southern Europe.

The flower heads of this have an action upon insects similar to that of insect powder. (Gieseler, Proc. Am. Pharm. Assoc., Vol. 10, 1862, p. 112.)

ADHATODA ADHATODA (L.) Lyons. *Acanthaceæ*. Synonyms: *Adhatoda vasica* Nees., *Justicia Adhatoda* L. Malabar Nut. India.

Fatal to flies, fleas, mosquitoes, leeches, the pupæ of aquatic insects, and even to frogs. (Rusby, Chemist & Druggist, Vol. 34, June 15, 1889, p. 831.)

ÆSCULUS GLABRA Willd. *Æsculaceæ*. American Horse-Chestnut, Ohio Buckeye. Eastern U. S.

<sup>2</sup>I would call attention to the meaning of the term "Insecticide" as defined in the Insecticide Act of 1910, Sec. 6: "That the term 'Insecticide' as used in this act shall include any substance or mixture of substances intended to be used for preventing, destroying, repelling, or mitigating any insects which may infest vegetation, man or other animals, or households, or be present in any environment whatsoever." Regulation 14 of "Rules and Regulations for Carrying Out the Provisions of the Insecticide Act of 1910" (U. S. Department Agr., Office of the Secretary, Circ. No. 34, 2d revision, August 24, 1917, pp. 5-6) defines an insect as follows: "The term 'insect' as used in the act and these regulations, is understood to mean any of the numerous small invertebrate animals generally having the body more or less obviously segmented, for the most part belonging to the class Insecta, comprising six-legged, usually winged, forms, as beetles, bugs, bees, flies, etc., and to other allied classes of arthropods whose members are wingless and usually have more than six legs, as spiders, mites, ticks, centipedes, wood lice, etc."

<sup>3</sup>We have used the botanical nomenclature as given by Britton and Brown, "The Illustrated Flora," 1913 edition, for plants native to this country, and the "Index Kewensis" for foreign genera and species.

Tested upon the cotton worm (*Aletia*) neither the alcoholic extract of the fruit nor the alcoholic extract and decoction of the leaves produced any effect. (Riley.)

*ÆSCULUS PAVIA* L. *Æsculaceæ*. Red or Little Buckeye. South-eastern U. S.

Bedsteads made of the horse-chestnut are said not to be infested by bugs. (Porcher.)

*AGAVE AMERICANA* L. *Amaryllidaceæ*. American Aloe, Century-plant. Tropical America.

The infusion of the leaves can be applied as an insecticide. (von Mueller.)

*AILANTHUS GLANDULOSA* Desf. *Simarubaceæ*. Tree of Heaven. China, cultivated in the U. S.

Prof. Meehan states that it checks the spread of the rosebug, to which the tree is destructive. (von Mueller.)

Some years since, when a caterpillar was stripping the oaks in front of my yard, I observed that some which had ascended an ailanthus tree (frequently called the tree of heaven) fell from it paralyzed and soon died. So, when the caterpillars attempted to cross my fence, I placed in their way, at short intervals, branches of ailanthus leaves, and killed immense numbers of them, effectually protecting my yard and garden. (Correspondent in Mississippi to Riley.) The decoction and infusion of the leaves produced no effect on cotton forms (*Aletia*). (Riley.)

*ALOE* L., sp. div. *Liliaceæ*. The resin is an insecticide. (Greshoff.)

*ALOE FEROX* Mill. *Liliaceæ*. South Africa. Inspissated juice of leaves. Cape Aloes.

The bitter sap, used for dressing wounds, keeps off flies, very effectually. (von Mueller.)

*ALOE VERA* (L.) Webb. *Liliaceæ*. Synonyms: *Aloe perfoliata* var. *vera* L., *Aloe vulgaris* Lam., *Aloe Barbadosensis* Mill., includes *Aloe indica* Royle and *Aloe littoralis* Koenig. Source of Barbadoes Aloes. India to northwestern Africa, nat. in West Indies.

Powdered Barbadoes aloes was on one occasion found quite as effectual as insect powder. (Mason in discussion of article by Kirkby, Pharm. J. & Trans., 3d Ser., Vol. 19, Sept. 22, 1888, 241.)

*AMANITA MUSCARIA* (L.) Pers. *Agaricaceæ*. Synonym: *Agaricus Muscarius* L. Fly Agaric. Europe.



As a fly poison it has been used in Europe for hundreds of years. (Chesnut, U. S. Dept. Agr. Div. Bot. Bull. 20, p. 13, 1898.)

AMANITA PANTHERINA. *Agaricaceæ*. Java.

Used as a fly poison. (Lyons.)

AMBROSIA ELATIOR L. *Ambrosiaceæ*. Ragweed. Eastern U. S. to British Columbia and Mexico.

The alcoholic extract and decoction produced no result upon cotton worms (*Aletia*). (Riley.)

AMBROSIA TRIFIDA L. *Ambrosiaceæ*. Great Ragweed. Ontario to Florida and Colorado.

The decoction, infusion and alcoholic extract produced no effect upon cotton worms (*Aletia*). (Riley.)

ANAMIRTA COCCULUS (L.) Wight & Arn. *Menispermaceæ*. Synonyms: *Anamirta paniculata* Colebr., *Menispermum Cocculus* L., *Menispermus lacunosum* Lam., *Cocculus suberosus* DC. Fruit = *Cocculus indicus*, fish-berries, India-berries. East Indies and Hindustan.

According to R. F. Bacon, the fruit is used in the Philippines for an antiparasitic ointment. (Greshoff. 1913.) Parasiticide (Lyons).

ANONA CHERIMOLIA Mill. *Anonaceæ*. Synonym: *Anona tripetala* Ait. Cherimolia. Peru.

The seed is used as an insecticide. (Greshoff.)

ANONA GLABRA L. *Anonaceæ*. Mexican Custard Apple.

Use similar to that of *A. reticulata*.

ANONA RETICULATA L. *Anonaceæ*. Custard Apple. West Indies.

The powder of the seed is employed as an insecticide and is dangerous. (Maisch, Am. J. Pharm., 4th Series, Vol. 15, July, 1885, p. 339.)

ANONA SPINESCENS Mart. *Anonaceæ*.

The seeds, either finely powdered or in the form of a decoction, are used as an insecticide. (Greshoff.)

The pulp is used as a fish poison and for the killing of vermin. (G. Dragendorff, Die Heilpflanzen, 1898, p. 216.)

ANONA SQUAMOSA L. *Anonaceæ*. Oriental Custard Apple. East Indies.

The seeds are used against head lice. (C. Hartwich, Die neuen

Arzneidrogen, quoted by Greshoff.) Seeds parasiticide. (Lyons.)

ANTHEMIS ARVENSIS L. *Compositæ*. Corn Chamomile. Europe, nat. in U. S.

The odor drives away mice and insects. (Greshoff, 1913.) The flowers of this were entirely inactive against flies. (Kalbruner.)

ANTHEMIS COTULA L. *Compositæ*. Synonym: *Maruta Cotula* DC. May-weed. Europe, nat. in U. S.

A decoction of the leaves of the plant it is said will destroy all species of insects. (Garrigues, Proc. Am. Pharm. Assoc., Vol. 19, 1871, p. 506.)

The powdered flower heads possess insect killing properties equal to that of Persian insect powder. The powder is very effective against bed-bugs, fleas and flies, but ineffective against grain worms and other caterpillars. Ants left their nest into which the powder had been blown. Plant lice resisted its effect the least of any of the insects. (Pharm. Ztschr. Russland, Vol. I, No. 23, April 1, 1863, p. 578.) The flowers of this were entirely inactive against flies. (Kalbruner.)

ANTHEMIS NOBILIS L. *Compositæ*. Synonym: *Chamomilla nobilis* Godr. Roman Chamomile. Europe, cult. and adv. in U. S. The flower heads = Anthemis U. S. P.

The flower heads have an action on insects similar to that of insect powder. (Gieseler, Proc. Am. Pharm. Assoc., Vol. 10, p. 112, 1862.) The flowers of this were entirely inactive against flies. (Kalbruner.)

ANTHEMIS TINCTORIA L. *Compositæ*.

The flowers of this were entirely inactive against flies. (Kalbruner.)

ARISÆMA DRACONTIUM (L.) Schott. *Araceæ*. Synonym: *Arum Dracontium* L. Green-dragon, Dragon-root, Dragon's Head. Canada and eastern U. S.

The corm is somewhat acrid and is used to destroy insects. (Pammel.)

ARISÆMA JAPONICUM Bl. *Araceæ*.

The root is used in Japan as an insecticide. (Greshoff, 1913.)

ARISÆMA TORTUOSUM Schott. *Araceæ*.

The root is used as an insecticide. (Greshoff.)



ARISTOLOCHIA CORNUTA Mast., ARISTOLOCHIA ORNITHOCEPHALA Hook. (=A. BRASILIENSIS Mart et Zucc.), ARISTOLOCHIA ELEGANS Mast. *Aristolochiaceæ*.

The flowers are fatal to insects. (Greshoff.)

ARTEMISIA ABSINTHIUM L. *Compositæ*. Synonym: *Absinthium vulgare* Lam. Wormwood. North Africa and Europe. Thoroughly established and common in E. Canada and N. New England. Elsewhere local. Naturalized from Europe.

Recommended for cultivation as a preventative of various insect-plagues, even the phylloxera. (von Mueller.)

ASAGRÆA OFFICINALIS (Ch. & Sch.) Lindl. *Liliacæ*. Synonyms: *Veratrum officinale* Ch. & Sch., *Schanocaulon officinale* Gray, *Helonias officinalis* Don, *Sabadilla officinarum* Brandt & Ratzeb. Sabadilla. Mexico to Venezuela.

The use of the seeds against lice is well known.

ASCLEPIAS CURASSAVICA L. *Asclepiadaceæ*. Bastard Ipecac. Tropical America.

It is used by the Indians of the Isthmus of Tehautepec (southern Mexico) to keep away vermin, especially fleas. They make a rough broom of it, and sweep the floors and walls of their huts, and find that they are not troubled with fleas for a considerable time afterwards. They have tried brushing dogs with it when their coats are full of vermin, and it appears to answer the same purpose with them. (Kew Bull. 130, Oct., 1897, p. 338.)

ATROPA BELLADONNA L. *Solanaceæ*. Deadly Nightshade, Belladonna. Southern Europe and Central Asia.

Decoction and alcoholic extract of leaves produced no effect on cotton worms (*Aletia*). (Riley.)

BAPTISIA TINCTORIA (L.) R. Br. *Fabaceæ*. Synonyms: *Sophora tinctoria* L., *Podalyria tinctoria* Michx. Indigo-weed, Shoo-fly. Eastern U. S.

The plants placed in the harness keep flies from horses. (Williams, Trans. Am. Med. Assoc., Vol. 2, 1849, p. 916.) The alcoholic extract and decoction produced no effect upon cotton worms (*Aletia*). (Riley.)

The fresh plant attached to the harness of horses keeps off flies—much used in Virginia for this purpose. There is no gum exuding from it and the odor is not pungent, but it seems to prove hostile to

them. I have noticed that they will not remain upon the plants. (Porcher.)

*CALADIUM BICOLOR* Vent. *Araceæ*.

The powdered leaves are used as an insecticide. (Greshoff.)

*CALLILEPIS LAUREOLA* DC. *Compositæ*.

The powdered root is used as an insecticide in Natal. (Greshoff, 1913.)

*CANNABIS SATIVA* L. *Cannabaceæ*. Hemp. Asia, cult. in U. S.

The hemp-plant serves as a protection against insects on cultivated fields, if sown along their boundaries. (von Mueller.)

*CAPSICUM* sp. L. *Solanaceæ*. South America; widely cultivated.

Undiluted capsicum killed cotton worms (*Aletia*) on contact after twelve hours. (Riley.)

*CARAPA GUIANENSIS* Aubl. *Meliaceæ*. Synonym: *Xylocarpus Carapa* Spreng. Andiroba or Carapa Tree. Guiana.

Decoction used as an insecticide. (T. Peckolt, 1901; quoted by Greshoff, 1913.)

*CASSIA OCCIDENTALIS* L. *Casalpiniaceæ*. Coffee Weed; Coffee Senna. Widely diffused in tropical countries.

Alcoholic extract and decoction. This has undoubtedly some effect on the worms (*Aletia*) though much less than the China tree berries. Appears to act upon contact, though very slowly. The worms appear to get affected several hours after application, resting motionless and without feeding, but were recovered on the second day. Some young worms were found dead one day after application, but it is doubtful whether from the effect of the decoction or killed by the force of the spray. (Riley.)

*CASSIA STIPULACEA* Ait. *Casalpiniaceæ*.

The leaves are used as an insecticide. (Greshoff.)

*CERATOTHECA INTEGRIBRACTEATA* Engl. *Pedaliaceæ*.

The decoction is used in West Africa as an insecticide. (Greshoff, 1913.)

*CHENOPODIUM AMBROSIOIDES* L. *Chenopodiaceæ*. Synonyms: *Ambrosia anthelmintica* Spach., *Orthosporum anthelminticum* R. Br., *C. ambrosioides* var. *anthelminticum* A. Gray. American Wormseed. Europe, nat. in U. S.

No effect whatever on cotton worms (*Aletia*) was observed from

the application of the alcoholic extract of the blossoms and green fruits. (Riley.)

CHROSPERMA MUSCÆTOXICUM (Walt.) Kze. *Melanthaceæ*. Synonyms: *Amianthium muscætoxicum* A. Gray, *Melanthium muscætoxicum* Walt., *Zygadenus muscætoxicum* Regel (Kew), *Helonias erythrosperma* Mx. and Ell. Sk. Fly-poison; Crow-poison. Eastern U. S.

"This plant is a narcotic poison, and is employed in some families for destroying the house-fly. The bulbs are triturated and mixed with molasses or honey, and the preparation is spread upon plates and placed in parts of the house most infested. The flies are soon attracted, and the poison takes effect while they are sipping it. They are perceived to stand unsteadily, totter, and fall supine. The flies, unless swept into a fire or otherwise destroyed, revive in the course of twenty-four hours." (Stephen Elliott, *A Sketch of the Botany of South Carolina and Georgia*, Vol. I, p. 421; Charleston, 1821.)

CHRYSANTHEMUM CAUCASICUM. *Compositæ*.

According to Bishop (U. S. Dept. Agr. Report, 1859) and Browne (ditto for 1858) Persian insect powder is made from this.

CHRYSANTHEMUM CINERARIÆFOLIUM Benth & Hook. *Compositæ*.

Synonym: *Pyrethrum cinerariæfolium* Trev. Dalmatian insect flowers. Dalmatia. Cult. in Japan and in California.

The powdered flower heads of this plant constitute the well known Dalmatian insect powder.

CHRYSANTHEMUM COCCINEUM, CHRYSANTHEMUM CORONIFOLIUM. *Compositæ*.

According to von Mueller, these yield the Persian insect powder.

CHRYSANTHEMUM CORONARIUM. *Compositæ*.

Flowers of this were entirely inactive against flies. (Kalbruner.)

CHRYSANTHEMUM CORYMBOSUM. *Compositæ*.

Flowers of this were very feebly benumbing to flies. (Kalbruner.)

A powder made from a mixture of unopened and opened flowers, dried in the sun, was slightly less effective than insect powder, against flies and ants. (Böhmer, *Pharm. Ztg.*, Vol. 40, No. 64, August 10, 1895, p. 523.)

CHRYSANTHEMUM FRUTESCENS L. *Compositæ*. Marguerite. Canary Island, cult. in gardens.



Landerer claims that one may advantageously replace ordinary insect powder with the flowers of this plant. (Jahresberichte für Pharmacie, 1879, p. 92.)

CHRYSANTHEMUM INDICUM. Persian Chamomile, Flea-grass or Flea-killer.

CHRYSANTHEMUM LEUCANTHEMUM L. *Compositæ*. Synonym: *Leucanthemum vulgare* Lam. Ox-eye Daisy. Europe and Asia, nat. in eastern U. S.

Flowers of this were entirely inactive against flies. (Kalbruner.)

CHRYSANTHEMUM MARSCHALLII Aschers. *Compositæ*. Synonyms: *Pyrethrum carneum* M. B., *Chrysanthemum carneum* Weber. See *C. roseum*.

CHRYSANTHEMUM PARTHENIUM (L.) Pers. *Compositæ*. Synonyms: *Matricaria Parthenium* L., *Pyrethrum Parthenium* Smith, *Tanacetum Parthenium* Schulz. Feverfew. Europe, adv. in U. S.

Flowers have a benumbing effect on flies, acting in 1 to 2 hours. (Kalbruner.)

Pulverized when dried and perfectly fresh it has an effect on roaches similar to that of insect powder, and appears to be very distasteful to them if dusted in their haunts. (Glover, Rept. U. S. Com. Agr., 1874, p. 133.)

CHRYSANTHEMUM ROSEUM Web. & Mohr. *Compositæ*. Synonym: *Pyrethrum roseum* Bieber. Persia to Caucasus Mountains.

The powdered flower heads of this or of *C. Marshallii* constitute Persian insect powder. In the Index Kewensis both species are referred to *C. coccineum* Willd. (Lyons.)

CHRYSANTHEMUM SEGETUM L. *Compositæ*. Synonym: *Pyrethrum Segetum* Moench. Corn Marigold. Europe.

Used in Greece in the same manner as the Persian insect powder, and is quite efficacious for the purpose, particularly when used in fumigation. (Landerer, Am. J. Pharmacy 4th series, Vol. 7, April, 1877, p. 155.)

CIMICIFUGA RACEMOSA (L.) Nutt. *Ranunculaceæ*. Synonyms: *Actinospora racemosa* L., *Cimicifuga Serpentina* Pursh, *Macrotrys actæoides* Raf., *Botrophis actæoides* Raf., *Thalictrodes racemosum* O. Kze. Black Cohosh, Black Snakeroot, Bugbane. Eastern U. S. Rhizome and roots = Cimicifuga U. S. P.

Powdered *cimicifuga* seemed to be devoid of insecticidal properties. Crickets (*Gryllus*) kept in contact with the powdered drug for hours showed no toxic effect. . . . As a fumigant *cimicifuga* proved unsatisfactory, acting more as an anæsthetic than as an insecticide. . . . The fluid extract of *cimicifuga* was tried, employing the contact method in open jar. This preparation of the drug proved more effective, killing the insects almost instantly, but it was also observed that alcohol alone (which is the menstruum used in the manufacture of the fluid extract) would produce practically the same result, although recovery was noted in some cases. Aqueous preparations of *cimicifuga* were ineffective. (Sayre, Trans. Kansas Academy of Science, Vol. 25, 1913, pp. 140-141.)

CITRULLUS COLOCYNTHIS (L.) Schrad. *Cucurbitaceæ*. Synonyms: *Cucumis Colocynthis* L., *Colocynthis vulgaris* Schrad. Colocynth. Asia, Africa and southern Europe.

The decorticated fruit = Colocynthis U. S. P. IX.

A decoction of colocynth serves as an insecticide. (Greshoff.)

CLEISTANTHUS COLLINUS Benth. & Hook. *Euphorbiaceæ*.

"The bark must contain some poison property, for not only do white ants leave it severely alone, but it is used here for poisoning fish. The inner bark placed on the sores of sheep and goats is efficacious in healing them and in destroying maggots." (W. F. Biscoe, Indian Forester, June, 1896, quoted by Greshoff.)

CRACCA sp. *Fabaceæ*. Synonym: *Tephrosia* Pers.

Warm and tropical regions.

U. S. Patent 1,242,954. A compound for use as an insecticide and sheep dip is formed from sulphur soap and comminuted *Tephrosia* (*Cracca*) plants, seeds or leaves. U. S. 1,242,955 specifies for the same purpose, a benzine extract of *Tephrosia* (*Cracca*) 0.5 to 1, soap 4, and dilute alcohol 15 parts.

CROTON FLAVENS. *Euphorbiaceæ*.

Used for the destruction of insects in Venezuela. Thoms found the dried plant to have no effect on roaches (*Blatta orientalis*) nor on flies nor gnats. (Thoms, Ber. der deutschen Pharm. Gesellschaft, Vol. 1, Heft 8, 1891, p. 241.)

CROTON TEXENSIS, CROTON GLANDULOSUS, CROTON CAPITATUS,

CROTON MONANTHOGYNUS. *Euphorbiaceæ*. Goat Weed.

The decoction from leaves and blossoms was without effect on cotton worms (*Aletia*). (Riley.)



DASYTOMA FLAVA (L.) Wood. *Scrophulariaceæ*. Synonym: *Gerardia flava* L. and Ell. Sk.

This plant, it is said, will prevent the attacks of yellow and other flies upon horses. (Porcher.)

DATURA STRAMONIUM L. *Solanaceæ*. Jimson-weed, Jamestown Weed. A cosmopolitan weed.

No result upon cotton worms (*Aletia*) was observed from the application of the alcoholic extract of the dried and ground seed or the alcoholic extract and decoction from leaves. (Riley.)

DELPHINIUM AJACIS L. *Ranunculaceæ*. Common garden larkspur. Southern Europe and cult. in gardens.

Listed as an insecticide by Greshoff.

DELPHINIUM BRUNONIANUM Royle.

Juice used to destroy ticks in animals. (Pharmacogr. Ind., quoted by Greshoff.)

DELPHINIUM CÆRULEUM Jacq.

Roots used to kill maggots. (Pharmacogr. Ind., quoted by Greshoff.)

DELPHINIUM CONSOLIDA L. Field Larkspur. Central Europe, cult. in gardens and adv. in U. S.

"A tincture, prepared by infusing an ounce of the seeds in a pint of alcohol . . . kills lice on the human head." (Williams, Trans. Am. Med. Assoc., Vol. 2, 1849, p. 875.)

"My friend, Dr. Carmichael, of Fredericksburg, Va., informs me that the tincture of the plant is destructive to insects, and usefully applied to the heads of children infested with them." (Porcher.)

"I have found the common larkspur an effective poison on insects." (Correspondent in Mississippi to Riley.)

DELPHINIUM STAPHISAGRIA L. Synonyms: *Staphisagria macrocarpa* Spach., *Delphinium officinale* Wenderoth. Lousewort. Mediterranean basin. Pliny mentions the use of the powdered seeds for destroying vermin on the head. (Porcher.)

DERRIS ELLIPTICA Benth. *Leguminosæ*. Malayan Fish Poison. Aker Tuba.

"It is used largely by the Chinese market gardeners as an insecticide, for which purpose the fresh roots are chopped up fine and

then pounded and mixed with water, which becomes milky, and which is sprayed or brushed over the plants with a bunch of feathers." (Leonard Wray, Pharm. J. and Trans., Vol. 52, July 23, 1892, p. 62.)

DERRIS ULIGINOSA Benth.

In India it is known to act as a poison upon worms and the larvæ of insects which trouble the cultivators, whence the Marathi name Kirtana, or "worm-creeper." (Proc. Am. Pharm. Assoc., Vol. 50, 1902, p. 322.)

DESMODIUM LABURNIFOLIUM DC. *Fabaceæ*.

The leaves are used as an insecticide. (Greshoff, 1913.)

DIARTHRON VESICULOSUM Endl. *Thymeleaceæ*.

DICHROPHYLLUM MARGINATUM (Pursh) Kl. & Garcke., EUPHORBIA MARGINATA Pursh. *Euphorbiaceæ*. White-margined Spurge. Minn. to Texas.

The decoction gave negative results when applied to cotton worms (*Aletia*). (Riley.)

An insecticide. (Burkill, quoted by Greshoff, 1913.)

DIOSPYROS MALACAPAI A. DC. *Ebenaceæ*.

The wood serves as an insect repellent. (Greshoff.)

(To be continued)

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## CHURCHILL'S TINCTURE OF IODINE.<sup>1</sup>

### HISTORY, EXPERIMENTS AND IMPROVED FORMULAS.

BY HERBERT C. RAUBENHEIMER, PHAR.D.

#### DISCOVERY OF IODINE.

Pharmacists not only helped in the development of their own profession but also that of medicine and chemistry. Little did Bernard Courtois, the French apothecary, when he discovered iodine in 1811, know of the great usefulness of this element and its preparations in pharmacy, chemistry and medicine.

Bernard Courtois was born in Dijon in 1777. He was apprenticed to the pharmacist Fremy at Auxere in 1804. On account of the great scarcity of natural saltpetre or potassium nitrate during

<sup>1</sup> Thesis submitted in course for degree.

Napoleon's wars, Courtois developed a process for the manufacture of artificial saltpetre or sodium nitrate. He employed the ashes of seaweed called varec, to make lye. He decomposed the extract of the ashes, which contained sodium carbonate with calcium nitrate and obtained a solution of sodium nitrate and a precipitate of calcium carbonate. He also discovered that when this was done in a copper boiler the solution attacked the metal. By further experiments he found out that the ashes of all seaweed had the same deteriorating effect on copper. Upon investigating this more thoroughly he discovered that after the crystallization of soda from the lye of kelp the remaining mother liquor when heated with sulphuric acid evolved violet vapors which sublimed into scales having a gray-black color and a bright metallic lustre. He also found out that when these were treated with ammonia a violent explosion resulted, and he noticed that the scales had a corrosive action on organic matter.

Courtois communicated his experiments to his friend Clement, who on November 20, 1813, read a report on this subject before the Academy of Sciences at Paris. Sir Humphry Davy was one of these present at this lecture and managed to obtain some of the bright metallic crystals. He made various experiments and finally concluded that this new substance was an element. The French chemist Gay-Lussac named the element iodine from the Greek "iodēs," which means violet-colored. However, Sir Humphry Davy got credit for the discovery of the elementary nature of iodine.

#### HISTORY OF CHURCHILL'S TINCTURE.

Churchill's tincture of iodine was originated by Dr. Fleetwood Churchill, the celebrated Dublin gynæcologist, professor and author, for use in his practice. He knew that iodine was a strong antiseptic and also had an astringent action and could be used successfully in gynæcology. But he needed a "soluble and stronger tincture," one which would readily mix with water and not have the iodine precipitated, as is the case with the ordinary tincture. Dr. Churchill then made the addition of potassium iodide which he found would keep the iodine in solution and prevent its precipitation so that the preparation would be soluble in water.



#### BIOGRAPHY OF DR. CHURCHILL.

Dr. Fleetwood Churchill was born in Nottingham in 1808 and studied medicine at Edinburgh. He received his M.D. degree in 1831 and then took a postgraduate course in gynæcology in Dublin. He finally settled in that city and acquired a very large practice in this branch of medicine. He was elected professor of gynæcology in the School of Physicians. He was president of the Dublin Obstetrical Society and also of the King's and Queen's College of Physicians. In 1851 the University of Dublin conferred the title of Doctor "Honoris Causa" upon him.

Dr. Churchill wrote text-books on "Diseases of Women," "Diseases of Pregnancy," on "Childbirth" and in 1841 published a book on "Researches on Operative Midwifery." He also translated very many valuable papers for the Sydenham Society. His numerous works were published in American editions and some were even translated into other languages. Besides being a noted scientist and doctor, Dr. Churchill was diligent in all sciences collateral to medicine. He was a great lover of books and an ardent supporter of foreign missions. He also was a member of the Dublin Microscopical Club. Dr. Churchill was one of those many-sided men, who was never afraid of being thought of as having nothing to do or to be neglecting his business because he was engaged in the works of philanthropy, charity or religion. He brought joy into the sick room, he played with the children and he sympathized with the sorrows of those who came into contact with him. Dr. Churchill retired in 1875 and died on January 31, 1878, in Ardtrea Rectory, County of Tyrone, Ireland.

Dr. Fleetwood Churchill of Dublin is not to be confused with Dr. John Francis Churchill of Paris who advocated the use of hypophosphites against tuberculosis.

#### FORMULA OF CHURCHILL'S TINCTURE.

Churchill's tincture of iodine first began to be used in this country about 1886. It was proposed for the first edition of the National Formulary, which was published by the American Pharmaceutical Society in 1888. The following formula was published first in the Preliminary Draft of the National Formulary, proposed by committee at the Providence, R. I., Convention, in Volume 34,



page 278, of the Proceedings of the American Pharmaceutical Association in 1886:

Iodine .....	75 grains.
Potassium iodide .....	15 grains.
Water .....	2 drachms.
Alcohol .....	6 drachms.

Churchill's original formula called for 75 per cent. alcohol, but by mixing the U. S. P. alcohol and water in the proportion given a 75 per cent. alcohol will be closely approximated.

Before going further it might be best to mention that this tincture should not be confused with liquor iodi causticus, or Churchill's iodine, the formula for which is published on page 248, Volume 34, Proceedings American Pharmaceutical Association, and consists of:

Iodine .....	120 grains.
Potassium iodide .....	240 grains.
Water .....	1 ounce.

It contains twice as much iodide as iodine and is much stronger in iodine content. This preparation was official in N. F. I, II, III, but not any more in N. F. IV.

The following formula for Churchill's tincture of iodine was published in 1888 in the first edition of the National Formulary of Unofficial Preparations:

Iodine .....	2½ Troy ounces.
Potassium iodide .....	½ Troy ounce.
Water .....	4 fluid ounces.
Alcohol, to make .....	16 fluid ounces.

The National Formulary II and III give the following formula for Churchill's tincture of iodine under the title *Tinctura Iodi, Churchill*:

Iodine .....	165 Gm.
Potassium iodide .....	33 Gm.
Water .....	250 Cc.
Alcohol, to make .....	1,000 Cc.

The same formula is official in N. F. IV, 1916, under the title of *Tinctura Iodi Fortior*, stronger tincture of iodine, with the synonyms *Tinctura Iodi, Churchill*; Churchill's tincture of iodine.

The *modus operandi* given is as follows: Dissolve the potassium iodide in water, then add the iodine and 600 milliliters of alcohol, and when all the iodine is dissolved add sufficient alcohol to make the product measure 1,000 milliliters.

It will be noticed that in all these formulas the ratio between the iodine and potassium iodide is five to one. There is five times as much iodine as potassium iodide. This is a larger proportion of iodine as compared with potassium iodide than found in any other tincture containing both ingredients.

#### CRITICISMS.

Criticisms have been made that the present formula is not satisfactory. All the iodine does not seem to be in solution and particles of it can be noticed in the bottom of the container. The fault must be that there is not enough potassium iodide to help to dissolve all the iodine.

#### EXPERIMENTS.

I have, therefore, based my experiments which are the original work in my thesis upon the three following questions:

1. How much iodine is dissolved in the present formula?
2. How much potassium iodide is needed to dissolve the official amount, 16.5 per cent. of iodine?
3. What other changes could be employed to make a satisfactory tincture?

All tinctures used in the experiments were made by the author in the Pharmaceutical Laboratory of the Philadelphia College of Pharmacy and were kept for various lengths of time before the determinations were made. One hundred mls of tincture were made in each case, as that was considered a fair sample. The tinctures were prepared according to the N. F. IV formula.

The assay for iodine consisted of the following procedure, which was carefully followed through all the experiments. "Mix 5 mls of the tincture with 25 mls of water and titrate with Tenth-Normal Sodium Thiosulphate Volumetric Solution. Each ml of Tenth-Normal Sodium Thiosulphate VS equals 0.01692 Gm. of Iodine, the factor in U. S. P. IX." As the sodium thiosulphate was not strictly tenth-normal the factor for it was obtained each day before it was used for a titration.

The assays were made in the Chemical Laboratory of the Phila-

delphia College of Pharmacy and the calculations were done according to the method of Professor Moerk. The references to percent. in this thesis mean the customary weight in volume percentage.

## I. IODINE IN SOLUTION.

The following are the results of the various experiments with the N. F. IV tincture:

A tincture assayed directly after preparation contained only 10.88 per cent. of iodine dissolved, which certainly shows the need of more potassium iodide.

One N. F. IV tincture was allowed to stand one week, another one and a half weeks and another three weeks before being assayed for the percentage of iodine. The one which stood one week showed only 12.13 per cent. of iodine in solution instead of the required 16.5 per cent. The tincture which stood one and a half weeks showed 14.97 per cent. of iodine with only a few granules remaining visible at the bottom of the bottle. The preparation which stood for three weeks before being assayed, showed that only 15.6 per cent. of iodine was taken up.

*Result.*—My experiments proved conclusively that there is not enough potassium iodide in the tincture to completely dissolve the entire amount of iodine.

## II. POTASSIUM IODIDE NECESSARY.

Experiments were then conducted by making new tinctures and adding different amounts of potassium iodide.

At first 1 Gm. of potassium iodide was added to 100 mls, making it 1 per cent. more of potassium iodide, a total of 4.3 per cent. After letting the tincture stand two days it was titrated and all the iodine was found to be dissolved.

The next assays were made with a tincture having one half Gm. of potassium iodide added to each 100 mls thus containing 3.8 per cent. A titration of such a tincture made right after it was completed showed 14.17 per cent. iodine content. A few such tinctures were set aside to note the effect of time upon the solubility of the iodine. Such a tincture containing 3.8 per cent. KI, showed 14.41 per cent. iodine dissolved on standing one week. On standing two weeks it showed 16.47 per cent. iodine dissolved, which is practically the entire amount.

The next experiments were made with a tincture containing 3.9 per cent. potassium iodide and this was found to dissolve all the iodine at once, as proven by titration immediately after preparation.

*Result.*—This led to a conclusion that the proper amount of potassium iodide to be added to the present N. F. tincture is between 5 to 6 Gm. per 1,000 mls.

Tinctures were then made containing 3.83 per cent., 3.85 per cent., 3.87 per cent. potassium iodide. The tinctures containing the 3.87 per cent. and 3.85 per cent. of KI contained the required 16.5 per cent. of iodide in solution right after making, while the 3.83 per cent. tincture showed it in three days.

#### PROPOSED IMPROVED FORMULAS.

This brought me to a conclusion that a tincture with either of the following two formulas could be used with better results than the present preparation of the National Formulary.

##### FORMULA No. 1.

Iodine .....	16.5	Gm.
Potassium iodide .....	3.85	Gm.
Water .....	25	mls.
Alcohol, to make .....	100	mls.

##### FORMULA No. 2.

Iodine .....	16.5	Gm.
Potassium iodide .....	3.83	Gm.
Water .....	25	mls.
Alcohol, to make .....	100	mls.

If the tincture is to be used right after dispensing, it is best to use the 3.85 per cent. potassium iodide, but if it is to be put away on the shelf until needed, as is the case in most drug stores, 3.83 per cent., potassium iodide will be sufficient.

#### ANOTHER MODIFICATION.

The author also made further experiments with various tinctures by eliminating part of the water and substituting alcohol for it. First a tincture was made containing the N. F. amount of potassium iodide made into a saturated solution and alcohol replacing the water which had been taken away. It was found that 15.24 per cent. of iodine was dissolved right after making and that in a tincture pre-



pared in such a way, after standing one week 16.47 per cent. of the iodine was dissolved. A tincture was then made with 3.5 per cent. of potassium iodide in enough water to make a saturated solution and all the iodine went in solution.

Therefore if a tincture is prepared according to the following formula:

FORMULA No. 3.

Iodine .....	16.5	Gm.
Potassium iodide .....	3.3	Gm.
Water .....	3	mils.
Alcohol, to make .....	100	mils.

it will be found to be stable and can be made more readily than the tincture containing the 25 mils of water because the alcoholic percentage has been increased which greatly helps to dissolve the iodine.

This last tincture should, of course, not be sold as Churchill's tincture of iodine as Dr. Churchill's original formula, as well as the present one, contains 75 per cent. alcohol, but the slight changes in it could easily be explained by the pharmacist to the various physicians in his neighborhood, who would understand the improved formula, and in a short time they would begin to write prescriptions for it and a large amount of such a tincture could be dispensed.

CONCLUSION.

The author has covered the three subjects, namely:

1. How much iodine is dissolved in the present formula?
2. How much potassium iodide is needed to dissolve completely the prescribed amount of iodine?
3. What other changes could be employed to make a satisfactory tincture?

The answers to these questions are fully presented in the thesis. In conclusion the author hopes that his feeble efforts to correct the faults of the present tincture will lead to more research work, and that a satisfactory formula will be published in the next edition of the National Formulary. This tincture has a large sale throughout various parts of the United States and work upon it cannot be neglected. Furthermore, inasmuch as the National Formulary is now a legal standard it is essential that its preparations are above criticism.

## THE NATIONAL PHARMACEUTICAL SERVICE ASSOCIATION: ITS PAST WORK AND FUTURE AIMS.

BY GEORGE M. BERINGER.

At the request of the Executive Committee, the following statement, reviewing briefly the activities of this organization, has been prepared for dissemination. It is very appropriate that at this time, the officers should present to the members and friends a résumé of the work in which this association has been engaged and the reasons for continuing, even more strenuously, our efforts. It may be considered as a report by the executive officers of the management and discharge of the duties assigned to them.

The National Pharmaceutical Service Association grew out of a meeting of medical practitioners held at the Philadelphia College of Physicians and Surgeons on Wednesday evening, June 20, 1917, to which a number of pharmacists had likewise been invited. At that meeting a number of the eminent physicians and surgeons present, whose age debarred them from active military service, decided to organize a medical Reserve Corps and through this to offer their professional services to the government during the war.

Recognizing that in civil practice, physicians depended upon the coöperation of the pharmacists and that pharmacy formed an important link in the ethical practice of medicine, this meeting of physicians adopted a motion suggesting that a similar reserve pharmaceutical corps be organized to coöperate with the medical corps in rendering efficient service to the government, if the need should arise. The following pharmaceutical and drug trade organizations of Philadelphia were represented at that meeting: The Philadelphia Branch of the American Pharmaceutical Association, The Philadelphia Association of Retail Druggists, The Philadelphia Drug Exchange, and the Philadelphia College of Pharmacy. The representatives of these organizations called a joint meeting of their members at the Philadelphia College of Pharmacy on June 25, at 8 p.m. to take action upon the suggestion emanating from the meeting of June 20, and to determine the best method of mobilizing the pharmaceutical interests to the support of the government.

It is a peculiar coincidence that the American Pharmaceutical Association was organized in the Philadelphia College of Pharmacy

in 1852, and that the National Pharmaceutical Service Association, sixty-five years later, owes its inception and organization to a meeting held in the same college. At this meeting it was pointed out that a medical reserve corps was a very appropriate organization to support the medical corps of the Army, but as no pharmaceutical corps was now established in the Army, a reserve pharmaceutical corps was not practicable.

The objects of this association as set forth in the preamble and constitution adopted,, are to mobilize all of the pharmaceutical interests to the support of the nation; to protect the lives and health of those in the military service of the country by providing supplies of dependable medicine and educated pharmaceutical service for the dispensing thereof; to develop the pharmaceutical service of the government according to the most advanced professional standard; to secure the establishment of a pharmaceutical corps in the U. S. Army, with ranking commensurate to the services rendered by the enlisted pharmacists; to improve the standing of the pharmacists in the Navy; to secure pharmaceutical representation on the Advisory Council to the Committee on National Defense; to coöperate with the government and the medical profession in providing the best medical attention for those in the service.

The growth of the association was comparatively rapid and its propaganda for the recognition of pharmaceutical service in the departments of the government has spread all over the country. It was at once seen that the army, with its preponderate need for men and for medical service, offered alike the greatest need and the greatest opportunity for approved pharmaceutical service. The absence of a pharmaceutical corps in the United States Army, although such corps have been established in most of the foreign armies and are rendering efficient service therein, has for many years been recognized as a defect in the medical department of our army and various pharmaceutical organizations, notably the American Pharmaceutical Association, have for years advocated the establishment of a pharmaceutical corps with appropriate rank as a branch of the medical department of the army.

An effort was made to obtain an interview with Surgeon-General Gorgas for the purpose of presenting the need for a pharmaceutical corps as a branch of the medical service of the Army. On July 24, 1917, a conference was held between a Board of Army Medical Officers appointed by the Surgeon-General and a committee com-



posed of Samuel L. Hilton, the Chairman of the Committee on National Defense of the American Pharmaceutical Association, and Eugene G. Eberle, Joseph W. England and Geo. M. Beringer representing this association. Pursuant to this conference, a formal brief was filed with the Surgeon-General setting forth in further detail, the work of the Pharmaceutical Corps in foreign armies and the need for such in the army of the United States. This brief was very widely circulated and has been the basis of many of the arguments in favor of a pharmaceutical corps in the army, that have since appeared in the pharmaceutical press, and newspapers of the country.

Shortly after the organization of the National Pharmaceutical Service Association, it was learned that Congressman George W. Edmonds of Pennsylvania, who in his earlier days had been a pharmacist, approved the objects of the association and the purpose to secure a Pharmaceutical Corps in the army and that he would be willing to introduce and further the passage of a measure having this in view. Thus, it became one of the first duties of your executive committee to prepare the draft of an act of Congress which was subsequently introduced in Congress as H. R. No. 5531 and commonly spoken of as the Edmonds Bill.

Quite naturally, a bill proposing such an innovation in the methods so long in vogue in the medical department of the United States Army met with some criticism and some opposition. The Surgeon-General was averse to such a reorganization of the medical department during the progress of the war. For the most part, the criticisms published evidenced prejudice, lack of knowledge of the duties of the pharmaceutical corps in foreign armies or a misunderstanding of the provisions of the Bill. Constructive criticisms are desirable so that any real defects in the measure may be corrected.

At the hearing held on the Edmonds Bill before the Committee on Military Affairs of the House of Representatives on March 19, 1918, this association was well represented and in addition to the verbal arguments, a formal brief was submitted which has likewise been published in the pharmaceutical journals.

From the first, your officers realized that the association was engaged in a campaign of education and that to arouse the public to the actual conditions under which medicines are supplied to the sick and wounded in the military service of the nation and the



moulding of public opinion whereby Congress would be compelled to authorize the modernizing of this branch of the medical service, and to assure to our soldiers the supervision and care of trained pharmacists for the dispensing of needed medicines, was no small task.

This propaganda has been carried on as extensively as the means at our command permitted. We have prepared and disseminated literature setting forth the service of pharmaceutical corps in foreign armies, especially the exemplary work of this corps in the armies of France, and the existing need for such service in our own army.

The indorsement of the movement by the American Medical Association was secured and its influential journal has editorially cordially favored the creation of a pharmaceutical corps as a need of the army medical service. A number of the other medical associations have likewise by resolution endorsed the Edmonds Bill and the medical journals have generally supported the movement. The national, state and local pharmaceutical associations have coöperated and the pharmaceutical press has devoted much space in energetically advocating our cause.

Thousands of our petitions have been distributed and scores of these signed by influential citizens have been filed with Congress. Hundreds of letters have been addressed to congressmen, senators and departmental officials urging the necessity for the proper dispensing of the medicines necessary to conserve the health of our soldiers. The campaign of education thus initiated has undoubtedly had considerable effect.

This association has been actively preparing and disseminating literature relating to the pharmaceutical service in the U. S. Army and many of the articles appearing in the public press have been inspired by our literature or the personal effort of members. It is safe to say that during the eighteen months that have elapsed since the organization of the National Pharmaceutical Service Association more has been done toward enlightening the American public on the lack of scientific pharmacy in the U. S. Army than had been accomplished in all the years of prior agitation on the subject.

The work of the National Pharmaceutical Service Association is not done. Although this war may be at an end, our efforts must not cease until an approved modern dispensing of the medicines and the best of medical attendance is assured to every man in our nation's army and navy and a proper recognition for the pharmacists en-

gaged in the government service is established. This necessity has long been recognized by some and is now understood and demanded by more of our people than ever before. The American people expect that their soldiers and sailors shall be given efficient medical attention, comparable at least with that which they received while in civil life and the increasing current of public sentiment to secure this end is marked and is a welcome indication of the progress of the propaganda and that our campaign of education has not been futile.

Every educational movement must be continued throughout a number of years before definite results are obtained and we may now consider that we are entering the second stage of our campaign. We recall that the Food and Drug Act became a law only after the agitation of a well-organized movement had been carried on for a quarter of a century. Of the final results of our efforts in behalf of a pharmaceutical corps in the U. S. Army there can be no doubt as our aims are along the lines of modern medical classification and scientific military progress that have already been adopted by most of the progressive nations.

The prospects for the enactment of a law embodying the principles contended for in the Edmonds Bill are brighter than ever before. Even though the Edmonds Bill has not been brought out of the Committee on Military Affairs and in deference to the wish of the previous Surgeon-General has not been acted upon, we know that many prominent and influential members of Congress have expressed themselves as favorable to the objects advocated and we believe that we are fully warranted in our opinion that the sentiment in this branch was so strong that the Bill would have passed the House if it had been voted upon.

Now that the war is over, the objection of the former Surgeon-General to a reorganization of the Medical Department of the Army no longer can hold. It is becoming more apparent that the attitude of that department was due to a misunderstanding of the desires of pharmacy and the purposes that a pharmaceutical corps in the army should serve and it is an important part of the duty of your officers and executive committee to explain away all grounds for such a lack of appreciation of the services that pharmacy can and will render the Medical Department of the Army if opportunity be afforded.

The reorganization of the Army and of its Medical Department is sure to receive the early consideration of Congress and in any

act reorganizing this branch of the army service the principles for which we have been contending must be incorporated. Our efforts are now being concentrated to secure in these reorganization laws a fair recognition of pharmacy and the establishment of a pharmaceutical corps, even though in the Army in peace times it be but a cadre that may be readily extended in times of need to the necessities of the nation.

This organization must be kept intact and actively continue the work that has been mapped out for it. It must maintain its energetic efforts and propaganda until the objects for which it was organized are achieved. To lose heart at this time, would mean the sacrifice of all of the progress that has already been made and destroy the hope of accomplishing the worthy objects and aims for which pharmacists have been contending for so many years and for the attaining of which the National Pharmaceutical Service Association was organized. To carry on this work to a successful conclusion this association must have the loyal support of the body pharmaceutic and its membership and its treasury should indicate no lack of interest on the part of the druggists of the United States.

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## THE EXAMINATION OF COMMERCIAL DEXTRIN AND RELATED STARCH PRODUCTS.<sup>1</sup>

BY F. W. BABINGTON, ALFRED TINGLE, AND C. E. WATSON.

The materials to be considered come under two heads, *viz.*, (1) starches that have been so treated as partly to hydrolyze a portion of the material, and (2) mixtures of untreated starches with starch that has been submitted to hydrolysis. Both classes of material may be treated analytically in the same way.

Starch furnishes many and ill-defined products when hydrolyzed, but for commercial purposes it often suffices to distinguish between, and determine, "starch" and "dextrin gum."

Our increasing but still incomplete knowledge of this branch of carbohydrate chemistry has caused the name starch to have a wider and more vague meaning than formerly, so that it is necessary to define the sense in which it is here used. Analytically we consider

<sup>1</sup> Reprinted from *Journal of the Society of Chemical Industry*, August 15, 1918.



as starch the carbohydrate or group of carbohydrates which, whether soluble in cold water or not, form a solution or gelatinize with hot water, give a blue color on treatment with iodine, and are precipitated by semi-saturation of the cold solution with barium hydroxide.

By dextrin gum is meant the mixture which results from the hydrolysis of starch when the change has not been carried so far as a complete conversion into sugars, though the latter may be present in the gum. "Dextrin gum" gives no blue color with iodine and is soluble both in cold water and in a cold, half-saturated solution of barium hydroxide.

The method of Lamb and Harvey<sup>2</sup> for the analysis of these mixtures is not satisfactory. It includes as "starch" only insoluble starch, while soluble starch is determined as part of the "dextrin." We have found that when the starch and dextrin are mixed in certain proportions it is very difficult to wash the former free from the latter with water; filtration is very slow and the starch passes into solution during the process to a serious extent. With reference to our first objection, we admit that for many commercial purposes it may be desirable to determine soluble starch among the dextrans. To adopt such a practice in our own laboratory, however, would not be satisfactory, as importers would thereby be penalized.

A method of examination which is both short enough for practical purposes and scientifically accurate is much to be desired, but for the present we have aimed at simplicity of procedure and a probable error of less than 5 per cent.

*Determination of Dextrin Gum.*—The sample (1 Gm.) is warmed in a 100 Cc. graduated flask, with 30 Cc. of water until just gelatinized, and cooled quickly; 50 Cc. of a cold saturated barium hydroxide solution is next added (the flask being meanwhile shaken), followed by enough water to bring the total volume to 100 Cc. The solution is filtered through a dry 15 Cm. paper and an aliquot portion (50 Cc.) of the filtrate is pipetted into a platinum dish. After the addition of 2 drops of a 1 per cent. phenolphthalein solution, *N/1* hydrochloric acid is added cautiously till the neutral point is just passed. A faint pink color is then restored by the addition of two or three drops of the barium hydroxide solution. A weighed quantity (about 10 Gm.) of sand is added, and the dish heated on a water-bath. The sand should be stirred when almost dry, to ex-

<sup>2</sup> *J. Soc. Dyers and Col.*, 1918, 34, 10; this JOURNAL, 1918, 133.

pose the maximum surface to the air, after which the dish is transferred to a well-regulated oven and dried to constant weight at 200° C., below which temperature crystallized barium chloride is dehydrated. Dextrin gum being hygroscopic, precautions must be taken accordingly. The dish is now heated strongly, but not beyond the temperature necessary for the complete combustion of the organic matter. During ignition the sand should be well stirred at intervals to allow full exposure to the air. The dish and contents are then cooled and weighed. The difference in weight before and after ignition represents the dextrin gum in 50 Cc. of filtrate, *i. e.*, in half the weight of sample taken.

*Limit of Accuracy.*—The phenolphthalein and the barium hydroxide added in excess of neutrality are obvious sources of irregularity, but if the amounts laid down above are not exceeded this is unimportant. A blank determination showed that the total resultant error from this source was 11 milligrams or 0.22 per cent. on the basis of a 1-Gm. sample.

The precipitation of starch by barium hydroxide is not quite complete, and that portion which remains in solution must ultimately be weighed as dextrin gum. The error likely to arise from this cause was found by making blank determinations of dextrin gum in two samples of starch. No. 1 was arrowroot and No. 2 a corn starch.

No.	Weight of Sample, Grams.	Weight of Dextrin Gum Found, Grams	Dextrin Gum Found, Per Cent.
1	1.00	0.0053	1.06
2	1.00	0.0087	1.74

Varying weights of arrowroot starch were added to measured volumes of a well-standardized dextrin solution and these mixtures were examined by this method, with results shown in the following table:

Mixture Number.	Weight of Starch Taken, Grams.	Weight of Dextrin in Solution, Grams.	Dextrin, Per Cent.	Total Weight of Dextrin Gum Found, Grams.	Dextrin Gum Found, Per Cent.
1	1.50	2.4879	62.3	2.4430	61.2
2	1.00	2.4879	71.3	2.3700	67.9
3	1.00	2.4879	71.3	2.5044	71.8
4	0.50	2.4879	83.2	2.4858	83.1

The error is thus within the limit aimed at, though much larger than would be tolerable for purposes of careful scientific enquiry.

Mixtures of unknown composition were next examined, all being ordinary articles of commerce. They were: (A) "Yellow dextrin"; (B) "Soluble starch"; (C) "Soluble gum" (a textile dressing); (D) "Treated starch" (believed to be a starch which had been washed with dilute acid). Each sample was examined independently by two analysts, so that differences in the result of duplicate analyses display all the error which can arise from "personal equation." The results obtained were as follows: Dextrin gum per cent. in (A) 99.90, 99.74; (B) 11.60, 11.86; (C) 24.00, 25.00; (D) 17.00, 15.72.

If dextrin gum is determined by the above method and determinations are also made of ash and moisture, the starch may then be estimated by difference. Such a procedure is not always desirable, and we have commenced work on a method for estimating the total starch directly, by means of the polarimeter, after hydrolysis. The pressure of departmental routine has prevented the completion of our experiments. At present is it enough to say that we have found that starch which has been precipitated by barium hydroxide is somewhat more rapidly hydrolyzed by hydrochloric acid than when not so treated. Whether the hydrolysis is complete we are not prepared to say, but we find that under our experimental conditions ( $100^{\circ}$  C. at atmospheric pressure) no further reduction in rotatory power can be observed after  $1\frac{3}{4}$  hours. Pending the completion of this work we suggest that the following determinations on such starch products as we have been considering will meet most commercial requirements: (a) Ash, (b) moisture, (c) dextrin gum by the method described here, (d) insoluble starch and (e) reducing sugars by some such method as that described by Lamb and Harvey (*loc. cit.*), (f) total starch by difference  $[100 - (a + b + c)]$ , (g) soluble starch by difference  $[f - d]$ , (h) non-reducing dextrin gum, by difference  $[c - e]$ .

Our method may also be applied to mixtures of starch and gum arabic, such as are sometimes met with commercially.

ANALYTICAL LABORATORY,  
DEPARTMENT OF CUSTOMS,  
OTTAWA.



CASTOR BEAN LOSSES, \$5,000,000; GOVERNMENT  
AID ASKED.<sup>1</sup>

A carload of hulled castor beans, the first to be shipped from the east coast, was sent to the government castor oil mill at Gainesville last week by Helm & Walker, whose hulling plant at West Palm Beach has been in operation for the last ten days. The carload of beans shipped last week contained about 800 bushels, and at the present government price of \$4.50 a bushel, had a value of \$3,600. Castor beans are being received at the local hulling plant from all points along the coast south of Titusville. The big hulling machine which cleans the beans and prepares them for crushing has an output of about 100 bushels a day.

It has been an open secret for some time that the big castor bean crop planted last spring at the request of the Aircraft Production Bureau is largely a failure, not only in Florida, but throughout the South. There were about 106,000 acres of castor beans planted under government contracts. Of this acreage, about 50,000 acres were planted in Florida, where it was supposed the beans would do exceptionally well because of the long growing season and semi-tropical climate. The beans were to be relied upon by the government to furnish a supply of castor oil for the lubrication of the airplane motors.

The estimates of government officers in charge of the crop were that the acreage planted would produce something more than 2,000,000 bushels of castor beans before January 1 next. Contractors and growers were induced to engage in the castor bean business upon the representation of officers of the war department and agricultural department that an average yield of from 20 to 40 bushels per acre might be expected.

Instead of the 2,000,000 bushels of beans anticipated from the big war-time crop, it is said that the total yield this year from the entire 106,000 acres throughout the United States will not exceed 500,000 bushels, and will probably be less. Along the east coast a few of the best fields have produced as high as from three to five bushels per acre, but the average field has been one bushel per acre and the crop on several thousand acres has been so poor that it has not been worth gathering.

<sup>1</sup> Reprinted from *The Florida Grower*, December 7, 1918.

Herman B. Walker, of Miami, one of the castor bean contractors, said recently that in all probability there will be an investigation by a committee of congress into the manner in which the castor bean crop was planted and managed.

"Fully 5,000 persons in Florida planted some acreage of castor beans in response to the government's request," said Mr. Walker. "It is doubtful if any one of these growers will receive enough for his crop to repay its cost. Many who planted a large acreage, depending upon the bean for their main crop, have been ruined by the failure, and in some cases will not be able to plant another crop of anything. The contractors, without exception, will lose heavily, not alone through failure of the yield to come up to expectations, but by reason of large and unexpected expenditures, not provided for in the contracts, which they have been required by the war department to make."

"Ninety per cent. of the crop shortage and loss to contractors and growers," declared Mr. Walker, "may fairly be attributed to the inferior seed, of unacclimated and unprolific varieties of castor beans, furnished by the government for the planting of the crop. Other contributing causes of the crop failure, have been the misinformation and bad advice furnished by the war department and department of agriculture, and damage caused by drought and flood.

"We all seem to have been the victims of hasty optimism on the part of the government officers in charge of the crop," said Mr. Walker. "The contractors are as badly victimized as the farmers. All our advertising and printing matter circulated to induce farmers to plant the crop, was approved by the government officers. They even censored our stationery. Not a single statement as to seed, prospective yield, cost of growing and probable returns, was made by our firm that was not made on the authority of responsible government officers.

"We were told that the seed to be furnished would be of the best varieties of beans and of superior quality. We found it to be mixed beans of uncertain age brought from India for crushing. There were beans of many better and more prolific varieties growing in Florida, but the government advice was that the native beans were not desirable. It was represented to us by Signal Corps officers that an average yield of from 30 to 40 bushels per acre might reasonably be anticipated, and that the crop would be highly profitable to both contractors and growers. In fact, these officers were so

certain of the big profits to be made out of the crop that they deprecated any appeal to patriotism in asking farmers to plant them, urging that at the price offered the growers would make so much money that there could be no credit given them for patriotism.

"Officers of both the war department and department of agriculture represented castor beans to be a crop that could be grown almost anywhere, on any kind of soil, without difficulty. One statement given the O.K. of these officers was that 'Castor beans will grow on any dry land in Florida.' Another statement similarly approved was that 'Any soil may be expected to produce 20 bushels per acre.'

"Army officers who inspected the crop required farmers to fertilize heavily and give expensive cultivation. In many cases the yield will not pay for the fertilizer. A bulletin issued by the department of agriculture announced that castor beans had 'no known insect or disease enemies.' As a matter of fact, army worms devastated thousands of acres; a hundred other kinds of bugs and worms have caused havoc, and thousands of acres have been ruined by a single fungus disease supposed by some pathologists to have been brought into the United States with the Indian seed. Thousands of acres of the beans failed to germinate because planters followed government advice to soak the seed in hot water, and large acreage was a failure because of other mistaken government advice concerning planting and culture.

"The present price makes it worth while for the farmers to pick their castor beans, but in many cases there will not be enough beans, even at the higher prices, to pay the cost of producing the crop, and in cases where there are no beans to show for large expenditures by the grower in money and work, no price, however high, will compensate the cost.

"It has been the policy of the government, in purchasing war supplies generally, to guarantee the manufacturer his cost and a fair margin of profit. Wages of war-workers have been generally high. There seems no good reason why a discrimination should be made against castor bean contractors and growers. It does not seem fair to ask them to bear the heavy burden of an unsuccessful experiment in growing a new crop from government seed, under government direction and supervision. We believe that the same liberal principle and policy should be applied to the castor bean crop that has been applied generally to other government contracts, and that where



losses on the part of contractors and growers have been sustained through following advice and directions, there should be reimbursement of such losses by the government, with a fair allowance for personal services or profits."

Mr. Walker estimates that Florida contractors and growers have lost \$5,000,000 or more this year, in money and labor, in trying to produce a crop of castor beans. The average losses will be scarcely less, he believes, in the other states where castor beans were grown under government contracts. These other states are Georgia, Alabama, Mississippi, Louisiana, Arkansas, South Carolina, North Carolina, Texas and California.

In view of the heavy loss entailed on southern farmers, and the wide area over which the failures and losses are scattered, Mr. Walker is of the opinion that congress will investigate the whole handling of the castor bean crop shortly, and will probably be asked to pass an appropriation bill for the relief of those who have suffered financially through the failure of the crop.—*Tropical Sun*.

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### THIRTEENTH MEETING OF THE NATIONAL PHARMACEUTICAL SERVICE ASSOCIATION.

A meeting of the National Pharmaceutical Service Association was held on Friday evening, December 20, at the Philadelphia College of Pharmacy. President Beringer, being unable to be present, because of sickness in his home, Vice-President Charles H. LaWall occupied the chair. The minutes of the previous meeting having been published, the reading, was on motion omitted.

The first order of business was to have been a presentation by the president of a brief résumé of the work of the N. P. S. A. during the year and a half of its existence, of the effort which the Association is making to secure recognition of professional pharmaceutical service in our military organizations. As Mr. Beringer was unable to be present, he requested that the publication of such a statement be authorized, and on motion, this request was approved.

The chief purpose for which the meeting had been called, was the consideration of the activities and future of the Hospital Corps of the United States Navy. Lieutenant Commander George F. Cottle, the head of the Hospital Corps, had, upon invitation, come

from Washington, to speak in the interest of the Corps. Lieutenant W. T. Minnick, Commandant of the Hospital Corps Unit, in training at the Philadelphia College of Pharmacy, had also consented to speak in the interest of the Corps. A number of lieutenants, and pharmacists in the Naval service, and also members of the corps in training at the Philadelphia College of Pharmacy were likewise present.

Lieutenant Minnick was called upon first and presented a brief statement, outlining the personnel of the corps as now existant, and the duties which the Naval Hospital Corpsmen are called upon to perform.

Lieutenant Commander Cottle then illustrated the work of the Corps by a number of lantern slides and drawings, showing the possibilities for advanced rating offered to members, by the present Naval regulations, and also the enormous growth of the organization during the present war. He also spoke of the splendid service rendered, under many trying conditions, by this branch of the service. The work of the Corps and its future, also the possibility for future recognition of members of this organization was discussed by Messrs. Howard B. French, Dr. D. Samuel Stout, Dr. C. B. Lowe, Prof. Gershenfeld, Dr. F. E. Stewart, Prof. J. W. Sturmer, and others.

Dr. Cottle in subsequent remarks, in answer to some of the comments, set forth the spirit which should animate those who seek service in the Corps in war times. The essence of his statement was that every American citizen undoubtedly wished to serve his country in some capacity during such a time of struggle as that which we have passed, and that, if his opportunity came through service in this Corps, then the question of mere personal advantage or rating rightly took a second place as compared with service to be rendered. He stated that it could not be expected that men without proper military training should immediately be given high ratings; that efficient Naval service required extensive military training, and that the opportunity to do one's bit in an honorable way had been welcomed by many men, and should be gratifying to the young men of a country. He called attention, however, to the fact that for men qualified both in professional and military subjects, there was provided abundant advancement, recognition and pay in the Hospital Corps, and that for men who had been in the service and had been prepared to assume the increased responsibility, recog-

niton, advanced rank, and larger opportunity for service, were given.

On motion, the meeting adjourned.

E. FULLERTON COOK,  
*Secretary.*

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## CORRESPONDENCE.

### PENNSYLVANIA WAR HISTORY COMMISSION.

PENNSYLVANIA COUNCIL OF NATIONAL DEFENSE AND  
COMMITTEE OF PUBLIC SAFETY.

WAR HISTORY COMMISSION

HEADQUARTERS:

HISTORICAL SOCIETY OF PENNSYLVANIA  
1300 LOCUST STREET  
PHILADELPHIA

December 19, 1918.

MR. GEORGE M. BERINGER,  
CARE OF AMERICAN JOURNAL OF PHARMACY,  
145 NO. 10TH ST., PHILA., PA.

*My dear Mr. Beringer:*—I thank you for your cordial letter of December 16th, and assure you that the War History Commission will appreciate the back numbers and the current issues of the AMERICAN JOURNAL OF PHARMACY.

The pharmacists of our State have performed many important services during the war and during the recent influenza epidemic. Our Commission would be delighted to have statistics concerning such activities and individual or personal descriptions of the war services of pharmacists. Perhaps a note to this effect in your JOURNAL might reach some persons interested in Pennsylvania, although, as I understand, your JOURNAL has a national circulation.

Yours sincerely,

ALBERT E. MCKINLEY,  
*Secretary.*

The Pennsylvania War History Commission was appointed by the Pennsylvania Council of National Defense and Committee of Public Safety in order to preserve a permanent record of Pennsylvania's part in the Great War



The commission is composed of the following:

Professor Herman V. Ames, Philadelphia. Professor of American Constitutional History University of Pennsylvania; Member of Advisory Commission, Division of Public Records, State Library.

The Honorable Hampton L. Carson, Philadelphia. Member of Pennsylvania Historical Commission.

The Reverend Doctor George P. Donehoo, Coudersport. Secretary, Pennsylvania Historical Commission.

Major General C. Bowman Dougherty, Vice Chairman, Wilkes-Barre. Formerly Commanding Division, National Guard of Pennsylvania.

Doctor John W. Jordan, Philadelphia. Librarian of Historical Society of Pennsylvania; Member of Advisory Commission, Division of Public Records, State Library.

Doctor Albert E. McKinley, Secretary, Philadelphia. Councillor of Pennsylvania Federation of Historical Societies, Professor of History, University of Pennsylvania.

Professor John Bach McMaster, Philadelphia. Professor of American History, University of Pennsylvania.

Doctor Thomas Lynch Montgomery, Curator, Harrisburg. State Librarian; Curator of Pennsylvania Historical Commission.

Mr. John E. Potter, Pittsburgh. Treasurer, Historical Society of Western Pennsylvania.

Colonel H. M. M. Richards, Lebanon. President, Pennsylvania Federation Historical Societies; President, Lebanon County Historical Society.

Honorable William C. Sproul, Chairman, Chester. Chairman, Pennsylvania Historical Commission.

Honorable William H. Staake, Philadelphia. President of Board of Commissioners on Uniform State Laws.

Mr. William H. Stevenson, Pittsburgh. Treasurer, Pennsylvania Historical Commission; President, Historical Society of Western Pennsylvania.

Mr. Christopher Wren, Wilkes-Barre. Corresponding Secretary, Wyoming Historical and Geological Society.

The commission has divided its membership into four General Committees to treat in detail various phases of war history:

*Committee on Military and Naval Records:* Messrs. Dougherty, Richards and Jordan.

*Committee on Legal, Constitutional and Political Records:* Messrs. Staake and Carson.

*Committee on Economic, Industrial and Financial Records:* Messrs. Stevenson, Ames, McMaster and Potter.

*Committee on Social, Educational and Religious Records:* Messrs. Donehoo, Wren and Montgomery.

#### DIVISIONS OF THE WORK.

The commission has divided its work into two principal divisions, as follows: (1) A record of all Pennsylvanians who have entered into the military or naval service of the United States or of any of the Allies. (2) A record of the commercial, industrial, and civic activities in Pennsylvania in war times.

#### COÖPERATION WITH OTHER ORGANIZATIONS.

The Pennsylvania War History Commission will coöperate in the collection and preservation of war records with County Councils of Defense, Local Historical Societies, Chambers of Commerce. Associations of War Welfare Workers, Religious Organizations, Educational Authorities, and Trade Organizations, both of employees and employers. It hopes that all such bodies will aid in furthering the work of preparing a complete record of Pennsylvania's participation in the war.

#### DOCUMENTS AND MATERIALS NEEDED FOR THE WAR RECORDS.

The following classes of documents and historical materials are needed by the commission. It will gladly preserve, file and care for them if they are deposited at the headquarters, 1300 Locust Street, Philadelphia.

(a) Personal records of Pennsylvania men or women who have gone into the service of the Army or Navy of the United States, the National Guard or Home Defense Leagues of Pennsylvania, or the military or naval service of any of the Allies. These records should include, where possible, photographs, a brief sketch of the person's life, and of his or her career in the service, letters from the front or camp, and similar materials.

(b) Minutes, official records, printed matter and circulars of all organizations performing war service. Most of this material will soon be lost or pass into the hands of private persons if it is not deposited in a place of safe-keeping.

(c) Diaries, autobiographies, war correspondence, and brief accounts of the participation of Pennsylvanians in the war.

(d) Newspapers and periodicals published in Pennsylvania during the war; and articles in papers outside the state bearing upon Pennsylvania and Pennsylvanians.

(e) Books, pamphlets, poems, and shorter articles bearing upon the War, written by Pennsylvanians.

(f) Reports of trade associations, corporation, firms and financial and industrial concerns upon war-time conditions.

(g) Documents bearing upon labor conditions during the war.

(h) Sketches of the history of specific industries or plants showing the steps in the adaptation to war needs.

(i) History of the war activities of Churches, Chambers of Commerce, Clubs, Red Cross, Y. M. C. A., K. of C., Y. M. H. A., Y. W. C. A., Emergency Aid, A. L. A., and similar organizations.

(j) Outlines of the history of the war work of Pennsylvania's financial bodies and institutions.

(k) Facts relating to agriculture and food production in war time.

(l) Sketches of the history of the war work of special classes of the population, as distinct from their participation in the general war activities of all citizens, *i. e.*, war work of women, of lawyers, of physicians, of dentists, of clergymen, of labor unions, of farmers, etc.

Correspondence and inquiries relating to the work of the commission should be addressed to the secretary, Albert E. McKinley, 1300 Locust Street, Philadelphia.

The AMERICAN JOURNAL OF PHARMACY will coöperate with this movement and similar efforts in so far as pharmacy is concerned. The activities of many pharmacists in the military service and likewise the equally important services of many of those associated with the drug trade in the numerous sustaining movements that have enabled our government to carry this war speedily to a successful termination should be properly and permanently recorded.

The editor will be pleased to receive items of interest, correspondence, data, suggestions or information relating to any phase of the efforts of druggists in behalf of the nation in this war period, and to collate and prepare such for the use of the various Federal and State war history commissions.



# THE AMERICAN JOURNAL OF PHARMACY

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## EDITORIAL.

### PHARMACEUTICAL RESEARCH.

The discussions now being carried on in various circles as to the necessity for endowed pharmaceutic research, exhibit a rather belated awakening of our people to the importance of pharmacy to mankind. It is but a tardy realization of the absolute necessity for a more thorough knowledge of the medicines supplied in the manifold services rendered by pharmacists.

The need for knowledge of remedial agents is not new. It has existed from the very entrance of sin in the world and the consequent ailments of mind and body. The information pertaining to drugs now at our command, is quite extensive and, if the sum of human knowledge was to be gauged by the volumes that have been published on this branch, it would be a veritable mountain. This accumulation is the result of the studies and researches of many generations. Piecemeal has been the construction of this monument commemorating alike the labors of the Galenists, the Paracelsians, the newer disciples of synthetic "coal-tar medication" and the advocates of biologic therapy.

The savants of all times and of all nations have added their investigations and discoveries. The followers of Hippocrates, the studious monks and the delving alchemists in their early endeavors pried from nature many secrets that are daily applied in medicine and pharmacy. The modern development of medicine, surgery and chemistry and the studies in bacteriology with the aid of research laboratories with ample equipment, have further evolved truths of inestimable value.

The student of the history of pharmacy is aware of the fact that pharmacists have contributed no small share of the volume of

scientific investigation and discoveries. In a measure it is their own fault, that the world at large is not better acquainted with the achievements that should rightly be accredited to pharmacy. The classic investigation of Liebig on the organic compounds of cyanogen and the accompanying isolation of the glucoside amygdalin and the ferment emulsin and the determination that the reaction between these was the source of benzaldehyde in oil of bitter almonds, is regarded as one of the most noteworthy contributions of this great scientist. Is it unfair to surmise that this problem was suggested to him during his early experience as an assistant to an apothecary?

From the pharmacists of every civilized country have emanated many contributions detailing able researches. These have come from many sources including the laboratories of the schools of pharmacy, those of the manufacturers and the dispensaries of individual druggists. The literature of pharmacy includes many such contributions that are of inestimable value in the practice of this time. There is no lack of evidence that scientific pharmacy has kept abreast of scientific medicine and chemistry and further that American pharmacists have contributed a fair share to this progress, although at times the investigations have been carried on under very adverse circumstances and without the aid of an endowment such as has amply provided for medical research.

In the past, the tendency among the more favored endowed research branches, such as medicine and chemistry, has been to ignore the claims of pharmacy for a distinct recognition as a proper field for systematic researches and to seek endowments that would permit of the study and development of this branch of modern medical service. The writer recalls his efforts when president of the American Pharmaceutical Association, to interest certain endowments in the coöperative work that pharmacy could perform and would perform in scientific investigations for the betterment of mankind, if the opportunity was afforded either for an independent endowment or for a share in the funds assigned for medical investigation. The claim then made that the medical endowment was in a position to take up independently any phase of pharmaceutical investigation was not then justified by the facts and has not since been demonstrated.

The work of the pharmacist and the service he renders to mankind is distinctly different from that of the physician, surgeon or chemist. It is true that with these, as well as with some other

professional workers, there are certain lines of common interest because of the multiplex articles that the pharmacist is compelled to handle and the various duties that he performs. Necessarily their studies of certain of the sciences is a common ground for coöperation and the coördinating of their efforts in behalf of scientific progress.

Modern differentiation and classification of the branches of medicine, however, assigns to pharmacy a distinct field of work, which while coördinating with medical practice and the work of the chemist in other fields, leaves to him the investigation of the collecting drugs, their study, preparation of medicines and modes of administration. The physician must know the actions of drugs in order to apply them intelligently in his practice, but to the pharmacist belongs the intimate knowledge of the drugs and the standardization and preparation of the medicines that will permit of their successful use by the physician. Each in his sphere performs important and necessary service to mankind and the professions that they represent are justified in seeking material aid in the efforts to perfect their knowledge and service to their fellow man.

The field of investigation and research open to pharmacists in the study of the numerous substances used for medication and the processes for the preparation of medicines and their exhibition is unlimited. Despite all of the accumulated information, many of our drugs, even some of those most extensively used, are as yet but imperfectly studied. Pharmacognosy, chemistry, testing, standardization, purification, manipulation, dispensing are some of the avenues opening up an inexhaustible field for research. The source of many of the commercial varieties of drugs is still unknown and the chemistry of some of the most important is still very largely an undisclosed secret of nature. Many of the statements, even those in our pharmacopœias and accepted text-book authorities are badly in need of investigation and verification. The problems awaiting systematic, scientific investigation, that can very properly be considered as exclusively within the province of pharmacy, are numberless.

It is encouraging to note that at least certain phases of pharmaceutical research have appealed to the large chemical interests. It has been proposed that there should be created through the efforts of the American Chemical Society a research institute with an endowment of several millions of dollars for the purpose of "co-



öperative study of the chemistry and pharmacology of synthetic organic chemicals, designed for medical use." Such an institute would very likely copy the methods used so successfully by the German manufacturers of synthetics for the determining of the actions and medical uses and likewise the commercializing of many of their chemical productions. No matter what are the interests back of this proposed research endowment, it should be encouraged to proceed along the lines stated. Possibly a means may be found by which pharmacists engaged in research may coöperate with this scheme of "coöperative study" and certainly such coöperation is to be desired for the benefit of all the interests concerned.

This movement of the American Chemical Society, recognizes the importance of investigation and research studies as applied to but one group of medicinal products and but a narrow branch of the large subject of pharmaceutical research. For this one section of the broader general research that should be covered by pharmacy, it is surmised that an endowment of millions of dollars is essential. This action serves to accentuate the necessity for a crystallization of the sentiment in favor of an endowed institution for pharmaceutical research that shall not be limited to only one phase of the possibility, but shall cover the entire field of necessity for comprehensive research within the limitations that should very rightly be assigned to pharmacy.

At the meeting of the American Pharmaceutical Association in Indianapolis in 1916, the proposition to inaugurate "An American Pharmaceutical Research Fund" was discussed with the thought that there was a possibility of uniting the various interests that might be concerned in such a movement in a combined effort that would yield ample endowment for the researches in the field of pharmacy that are so essential to the public welfare and to the progress of science. The result was the establishment of the American Pharmaceutical Association Research Fund with a committee of the association appointed to supervise the work. Doubtless this committee will do everything that is within its power and the limited funds at its command to stimulate research work in pharmacy and we may expect results from their efforts. But has not the association by its limited view of the possibilities limited and curtailed in advance the results that are possible.

May our preachments for a broader view among pharmacists themselves be not in vain.

G. M. B.

## OUR BOYS ARE COMING BACK.

Now that our boys in the khaki uniforms have performed their work over there so expeditiously and so effectively that "it's over, over there," new problems confront them and likewise those, who from necessity, were compelled to "keep the home-fires burning." With smiles we drowned the yearnings of the hearts as we cheered them on to the victory. Cheerfully we assumed the added labors due to a diminished force and labored and saved and gave for the triumph of our cause.

Now that peace is in sight and our boys are coming back we prepare to take up the new problems of reconstruction. It is the nation's duty to find employment, to reestablish the returning soldiers and sailors in useful vocations. The sooner we engage in intensive cultivation of our soil, the sooner the busy buzz of the factory and shop, the sooner full energy of commerce and industry and of education be reestablished the sooner the happiness of our people will be assured and the greater will be the prosperity of our country.

Our special interest is, of course, to aid the drug trade in the problems affecting this branch of vocational service. That the druggists of the country have been greatly inconvenienced by the lack of sufficient assistants and that many of the pharmacists and assistants to pharmacists by reason of their military service will be out of employment in their usual vocation is too well known to require any further comment. Many of these student assistants were not permitted to complete their educational requirements for registration as licensed practitioners of pharmacy. The prompt getting together of the employer with those seeking locations and the providing the means for the completion of the education of those whose course was interrupted so that they may become properly accredited pharmacists in their several states, are immediate problems of the period of reconstruction calling for our action.

Very properly the American Pharmaceutical Association has taken up this work and through the Advisory Committee of the A. Ph. A. for Soldier and Sailor Pharmacists is trying to solve many of the questions that will necessarily arise and here the American Pharmaceutical Association is again performing a signal service for the nation as well as for pharmacy. We bespeak the earnest coöperation of all bodies pharmaceutic as well as the support of the indi-

vidual druggists in the work of this committee which is under the able chairmanship of Frank H. Fredericks, No. 1005 Mercantile Library Building, Cincinnati, Ohio. If you are in a position to assist the committee in their work, in any way whatever, do not fail to communicate with the chairman.

The Philadelphia College of Pharmacy has likewise appointed a committee with Prof. Freeman P. Stroup as chairman to consider not only the question of the reestablishment of its own graduates who have been in the military service, but likewise to coöperate with the Committee of the A. Ph. A. and any other organizations or movements having as the object in view the assisting of soldiers and sailors to secure employment in the drug trade or allied industries.

G. M. B.

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## HYOSCYAMUS NIGER.

BY GEORGE P. KOCH, PH.D.

### INTRODUCTION.

Due to the fact that many crude drugs cannot be secured from foreign countries at the present time, the cultivation of medicinal plants in the United States has been greatly stimulated. In as much as the methods of propagation of the various medicinal plants are still quite imperfect, much research is still necessary in order that such crops may be grown successfully. Several investigators have worked on various phases of the medicinal plant culture, but as yet there seems to be an insufficient amount of data available by which a more or less inexperienced individual can go ahead and be successful in the production of such a crop. A very important factor in growing medicinal plants in the United States, where the cost of labor is so great, is the application of methods whereby such crops can be grown on a comparatively large scale, thus bringing into play the use of labor saving implements as much as possible (4).

The production of a crop running as high as possible in alkaloids and securing this crop as cheaply as possible, determines the extent to which such procedures would be successful. In commercial culture, *Hyoscyamus niger* seems to be a plant with which the greatest amount of difficulty has been experienced, and as yet, is grown very little in this country. Stockberger (10) contends that



"With very few exceptions, recent attempts to cultivate henbane as a drug crop in his country have resulted in failure." With the above thoughts in mind the author has made rather detailed study covering most of the phases of growing and developing *hyoscyamus*, *belladonna* and *digitalis*. The results considered in this paper refer only to the work with *hyoscyamus*. The results of the investigation with *belladonna* and *digitalis* will be presented in another series of papers (5, 6).

#### GERMINATION OF SEEDS OF *Hyoscyamus niger*.

The variability of seeds is always a very important factor. The only satisfactory method of determining viability is by germination tests. How long a time does it require for the seeds of *Hyoscyamus niger* to germinate? Newcomb (7) states that the seeds of the biennial variety of *Hyoscyamus niger* germinate in about four to six weeks, while the seeds of the annual variety germinate in from eight to ten days.

To secure more information on the germination of the seeds of *Hyoscyamus niger*, two samples of seed of the annual variety were tested. The blotter method, which is usually employed for testing seeds, was used. Two one hundred seed lots of each sample were counted out and the extent of germination noted. The results as tabulated below are the average of two determinations.

TABLE I.

SHOWING PERCENTAGE OF GERMINATION OF SEEDS OF *Hyoscyamus niger* ON VARIOUS DAYS.

Sample No.	Number of Days After Seeds were Planted											
	4	5	6	7	8	9	11	12	15	18	21	23
9	6	11	27	48	66	71	71	73	73	73	73	73
10	22	24	40	77	93	93	94	95	95	95	95	95

Upon observing the results as presented in the above table, it will be seen that most of the viable seeds will have germinated in from nine to eleven days.

Determining the viability of *Hyoscyamus niger* seeds between blotters or filter paper is very satisfactory but is limited, and the practice of germinating seed in the soil in conjunction with the blotter method, seemed quite advisable.

All soils contain a large number of weed seeds, some of which germinate very quickly, and thus interfere with germination tests. The soils also contain an abundance of spores of various destructive organisms, in particular, the "damping off" fungi. Sterilizing the soil by heat under pressure is the most satisfactory method of destroying these destructive agencies.

It had been previously shown in germination experiments with belladonna seeds (5) that by increasing the humidity and preventing excessive evaporation, the percentage of germination was very much larger than where these factors were not considered. With the above thoughts in mind, the following experiment was carried out. Into four flats, dimensions 12 by 20 inches, 25 per cent. compost soil was placed to within one inch of the top. A thin layer, about one fourth on an inch, of sand was sieved over the soil. The contents of the flats were saturated with water. Two of these flats were carefully wrapped with heavy manila paper and then sterilized in the autoclave at 15 pounds pressure for three hours. After this treatment, one flat was planted with one thousand hyoscyamus seeds of sample no. 9, and the other, with one thousand seeds of sample no. 10. Likewise, the two unsterile flats were planted with the same number of seeds of nos. 9 and 10, respectively. All the flats were covered with glass plates and placed in the greenhouse. The soil was kept moist by wetting slightly whenever necessary.

The number of seeds germinating during a period of three weeks was ascertained at intervals of one week. The germination of the samples of *Hyoscyamus* seeds in this experiment are recorded below.

TABLE II.  
SHOWING THE PERCENTAGE OF GERMINATION OF SEEDS OF *Hyoscyamus* IN  
STERILE AND UNSTERILE SOIL IN FLATS.

Sample No.	Treatment.	Days After Seeds were Planted.		
		7	14	21
9	Unsterile	5.7	8.1	7.9*
9	Sterile	20.1	32.6	33.8
10	Unsterile	14.0	16.8	10.3*
10	Sterile	30.9	37.1	31.9

\* Low results due to "damping off" fungi.

The results of the experiment as presented in the above table show that in the sterilized soil, the conditions were such that from

three to four times as many seeds germinated as where the soil was not sterilized. On comparing the results as shown in Table I with those in Table II, we find a great difference in the relative number of seeds germinated by the two methods. In the case of sample no. 9, 48 per cent. germinated by the blotter method while only 5.7 per cent. germinated in the unsterile soil, and 20.1 per cent. in the sterile soil. While in the case of sample no. 10, 77 per cent. germinated in seven days by the blotter method, and 14 and 30.9 per cent., respectively, germinated in the soil. It is true that when germination is determined by the soil method, the sprouts must appear through the thin layer of sand that covers the seeds, hence, it would probably take a longer period of time to see the sprouts than when the seeds are tested between blotters or filter paper. The destructive effects produced by "damping off" fungi are very apparent in the unsterilized soil by noting the results of the germination of samples nos. 9 and 10 on the twenty-first day.

To hasten and increase the germination of seeds of various kinds, usually those with hard coats, treatments with sulphuric acid and freezing are sometimes recommended. Newcomb and Haynes (8) found that by treating the seeds of the biennial variety of *Hyoscyamus niger* with concentrated sulphuric acid proved beneficial to germination, in that the results were much more uniform. To determine to what extent physical and chemical treatments were effective in hastening and producing more uniform germination of hyoscyamus seed, an experiment entailing these particular factors was made. One sample of hyoscyamus seed was moistened and then frozen at  $-12^{\circ}$  C. for four hours. Another sample was treated with concentrated sulphuric acid for  $2\frac{1}{2}$  minutes, the acid was quickly washed off, and the seed, about 5 Gm., was quickly washed with a liter of water. Flats of soil were sterilized as before. One flat was planted with one thousand of the original untreated seed; a second, with one thousand frozen seeds and a third, with a like number of the acid treated seeds. The flats were covered with glass plates and kept moist. After 21 days, the seedlings resulting from the germination of the seeds were counted. The results are presented below.



TABLE III.

SHOWING THE EFFECT OF VARIOUS TREATMENTS OF *Hyoscyamus* SEED ON THE PERCENTAGE OF GERMINATION.

Treatment	Percentage of Germination
Untreated seeds .....	2.4
Frozen seeds .....	4.0
Acid treated seeds .....	1.5

The results above show that freezing the seeds was effective in increasing the germination, while treating them with sulphuric acid produced no beneficial effects.

#### EFFECT OF INORGANIC FERTILIZERS UPON THE GROWTH AND DEVELOPMENT OF *Hyoscyamus niger*.

With such an expensive crop as hyoscyamus, it is quite essential that the correct fertilizing treatments are made. The extent to which fertilizers are effective in increasing the yield of hyoscyamus was determined.

The methods and fertilizer applications which were employed in the experiment follow. The soil used was that of a clay loam, which was the result of the disintegration of mica schist rock formation. This soil was taken from the upper five inches, namely, the surface soil, from the premises of the Mulford Biological Laboratories, at Glenolden. Four hundred and fifty grams of this soil was weighed and placed in each of eighteen 4-inch pots. The amounts of fertilizers applied were as follows: calcium carbonate 1,000 lbs.; calcium acid phosphate 800 lbs.; potassium sulphate 400 lbs.; sodium nitrate 600 lbs.; and magnesium sulphate 100 lbs., per acre of 2,000,000 lbs. Each determination was made in triplicate. The moisture conditions were maintained at the physical optimum of the soil, each pot being carefully weighed every morning and the loss of moisture restored with distilled water. Each pot was planted May 15, 1918, with a small plant, approximately 3½ to 4 inches high. Plants of as nearly the same size as possible were planted in the various pots, thus preventing every possible source of error. The plants, most of which were blooming, were harvested on August 12, 1918. The stems of the plants were cut off near the surface of the ground. The leaves and stems of each plant were placed in manila bags and dried at 90 degrees C. The results of the effects of the fertilizers upon the growth of hyoscyamus are shown below:

TABLE IV.

EFFECT OF VARIOUS FERTILIZERS UPON THE GROWTH OF *Hyoscyamus niger*.

Pot No.	Fertilizer Treatment	Wt. of Dry Material in Gms.	Average Wt. in Gms.
801	No fertilizer	1.6	
802	"	1.7	
803	"	1.7	1.66
804	Complete fertilizer*	2.1	
805	"	2.3	
806	"	4.2	2.80
807	Complete— $\text{Ca}(\text{H}_2\text{PO}_4)_2 \cdot 2\text{H}_2\text{O}$	1.9	
808	"	0.9	
809	"	0.5	1.10
810	Complete— $\text{K}_2\text{SO}_4$	2.2	
811	"	3.1	
812	"	2.2	2.50
813	Complete— $\text{NaNO}_3$	2.1	
814	"	2.3	
815	"	1.7	2.00
816	Complete— $\text{CaCO}_3$	2.7	
817	"	1.2	
818	"	2.3	2.20

\* Complete fertilizer represents 1,000 lbs.  $\text{CaCO}_3$ , 800 lbs.  $\text{Ca}(\text{H}_2\text{PO}_4)_2 \cdot 2\text{H}_2\text{O}$ , 400 lbs.  $\text{K}_2\text{SO}_4$ , 600 lbs.  $\text{NaNO}_3$ , and 100 lbs.  $\text{MgSO}_4$  per acre.

Applying a complete fertilizer to this soil greatly increased the yield of *Hyoscyamus niger*, as seen in comparing the weights of plants of pots nos. 804, 805 and 806 with 801, 802 and 803. Calcium phosphate seems to be the most necessary fertilizer required for the maximum growth of this plant as seen in determinations 807, 808 and 809. With this soil  $\text{K}_2\text{SO}_4$  seemed to be the least necessary for the maximum growth of the plant. Likewise, the absence of calcium carbonate did not result in materially reducing the yield of *Hyoscyamus niger* than where it was supplied.

#### CONTROL OF INSECTS.

In the cultivation of *Hyoscyamus niger*, the principal factor to be considered is the control against the attack of chewing insects. Stockberger (9) summarizes as follows: "the leaves of henbane usually suffer severely from the attack of the potato beetle, especially during the first year, and the crop is very likely to be destroyed if grown within range of this insect." Newcomb and Haynes (8) state that hyoscyamus is very susceptible to the attack of the Colorado potato beetle, but conclude that these may readily be controlled by early application of Paris green or other arsenical

poisons. Similarly, Borneman (1) stated that these plants should be sprayed about every day, as the potato bugs would devour them in one day. Farwell (3) concluded that the lack of success in commercial culture of *hyoscyamus* is the large cost in keeping the plant free from bugs.

Since it was difficult to keep *Hyoscyamus niger* free from chewing insects, a series of experiments were made to ascertain what spray mixtures could be employed that would keep the insects off the plants, and still not be injurious to the plant tissues. As a preliminary experiment, 15 large *Hyoscyamus niger* plants were selected. These, as yet, had not been attacked by any insects. Three plants were sprayed with arsenate of lead (5 lbs. 100 gal.); three, with Paris green (1 lb. 100 gal.); three were dusted with flowers of sulphur, and six were kept as controls, or untreated. The plants were sprayed on May 22, 31, and again on June 6, and the effects of the insects was carefully watched. The results are presented in the following table:

TABLE V.

SHOWING THE CONTROL OF THE PLANTS OF *Hyoscyamus niger* AGAINST THE ATTACK OF INSECTS.

Plants No.	Treatment.	Results.
1	No treatment.	Almost entirely destroyed.
2	" "	Entirely destroyed.
3	" "	Entirely destroyed.
4	Arsenate of lead.	Plants fine, few small holes in leaves.
5	" " "	Plants fine, few small holes in leaves.
6	" " "	Plants fine, few small holes in leaves.
7	Paris green.	Plants destroyed by spray.
8	" "	Plants destroyed by spray.
9	" "	Plants destroyed by spray.
10	Sulphur	Little injury, lower leaves destroyed.
11	"	Little injury, lower leaves destroyed.
12	"	Little injury, lower leaves destroyed.
13	No treatment.	Almost entirely destroyed.
14	" "	Almost entirely destroyed.
15	" "	Entirely destroyed.

From the foregoing results, it is very apparent that *hyoscyamus* plants must be sprayed in order to control insects, as in every case the control plants were either partially or entirely destroyed. Arsenate of lead was very effective in controlling the insects, and



TABLE VI.  
SHOWING THE EXTENT TO WHICH VARIOUS SPRAYS CONTROLLED LEAVES OF *Hyoscyamus niger* AGAINST THE ATTACK OF THE  
COLORADO POTATO BEETLE.

Plant No.	Spray Treatment	Presence of Beetles	Results After 24 Hours		Results After 70 Hours	
			Condition of Beetles	Condition of Leaves	Condition of Beetles	Condition of Leaves
1	No treatment.	No beetles.	—	No injury.	—	No injury.
2	" "	Beetles added.	Very active.	Leaves entirely eaten.	Very active.	As noted before.
3	" "	" "	" "	" "	" "	" "
4	Arsenate of lead.	No beetles.	—	No injury.	—	No injury.
5	" "	Beetles added.	Dead.	Two small holes in leaves.	Dead.	As noted before.
6	" "	" "	" "	About $\frac{1}{10}$ leaf destroyed.	" "	" "
7	Paris green (1-150).	No beetles.	—	No injury.	—	No injury.
8	" "	Beetles added.	1 dead.	About $\frac{1}{7}$ leaf destroyed.	Dead.	$\frac{1}{6}$ of leaf surface eaten.
9	" "	" "	Dead.	" $\frac{1}{6}$	" "	Same as before.
10	Paris green (1-300).	No beetles.	—	No injury.	—	No injury.
11	" "	Beetles added.	1 dead.	$\frac{1}{4}$ of leaf surface eaten.	Dead.	Same as before.
12	" "	" "	1 "	$\frac{1}{6}$ " "	1 dead.	" "
13	Sulphur.	No beetles.	—	No injury.	—	No injury.
14	" "	Beetles added.	Very active.	$\frac{1}{4}$ of leaf surface eaten.	Very active.	$\frac{3}{4}$ of leaves eaten.
15	" "	" "	" "	$\frac{1}{4}$ " "	" "	" "

at the same time, was not injurious to the plant. Paris green (1-100) was too concentrated for hyoscyamus, as six days after it had been applied, all three plants were dead, as the result of injury from spraying. Up to a certain period, flowers of sulphur proved fairly effective in controlling the insects. After that time, they became accustomed to the sulphur, and hence, it did not combat the insects. The Colorado potato beetle was the most destructive insect.

To gain more information on the effect of the various sprays in controlling the Colorado beetle, another series of experiments was carried out under controlled conditions. To each of eighteen sterile petri dishes, either one large or two medium sized portions of leaves of hyoscyamus were added. The leaves of three petri dishes received no spray treatment. The leaves of three dishes were sprayed with arsenate of lead (5 lbs. per 100 gal. of water); three, with Paris green (1 lb. per 150 gal. of water); three, with Paris green (1 lb. to 300 gal. of water); and three, with flowers of sulphur. Into two petri dishes of each series of three, two potato beetles (one large and one of medium size) were placed. After 24 hours and again after 70 hours, the petri dishes and their contents were carefully examined and the results recorded.

As demonstrated in the preceding table, arsenate of lead was the most satisfactory in controlling the potato beetles, as it required but a small amount of this poison to destroy these insects. Both dilutions of the Paris green were effective, but it required a longer period of time to destroy the beetles, and a considerably larger amount of the leaves were destroyed where the Paris green was applied, than where the arsenate of lead was employed. Flowers of sulphur was entirely unsatisfactory, as a means of controlling the beetles, as shown on the second examination (70 hours after the insects had been in contact with the leaves), the beetles had almost entirely destroyed the hyoscyamus leaves, and the bugs were still very active. The rapidity with which the beetles destroy the leaves is appreciated in the results as shown in plates no. 2 and no. 3. In these cases where the leaves were not sprayed, the entire leaves were destroyed in 24 hours.

To ascertain how long Colorado potato beetles could remain alive when given no food, six beetles (two large, two of medium size and two small) were placed in a sterile petri dish, and their activity was noted. The result is shown in table below:

TABLE VII.  
SHOWING THE ACTIVITY OF SIX COLORADO POTATO BEETLES WHICH WERE ALLOWED TO REMAIN IN A PETRI DISH AND RECEIVING NO FOOD.

Kind of Beetles	Activity 24 Hours	Activity 70 Hours	Activity 77 Hours	93 Hours	100 Hours	167 Hours	223 Hours	238 Hours
Two small	Very active	Both 1/2 original size	Both alive	Both dead *	One alive	Both dead	I dead	Both dead
Two medium	" "	" " "	" "	One "	Getting smaller	" alive		
Two large	" "	" " "	" "	Both alive				

\* Both beetles eaten up by the others, as only the heads remained.



The above experiment shows conclusively that the potato beetles can live for a long period of time without receiving any food. Their size diminishes gradually during their period of fasting, and they decrease to less than one third of their original size before they die. It shows that the larger beetles can withstand the lack of food much better than the smaller ones. It also demonstrates the fact that potato beetles will utilize their own kind as a source of food when necessity demands it.

#### SEED FORMATION.

Since it was found very difficult to secure seeds of *Hyoscyamus niger* from the various possible sources, the extent of seed formation and selection were studied. To determine the effect of the stage of maturity of the seeds upon their variability, seeds were collected from plants at various periods. After they were dry, germination tests were made by the blotter method as mentioned above. Four samples were considered in this experiment. Sample no. 1 was collected on June 21, 1918, and sample no. 2, on June 25, 1918. The plants from which these seeds were taken were large and branching. The leaves and seed pods were still green. Some of the seeds in the pods were white in color, but most of them were beginning to turn brown. Samples nos. 9 and 10 were collected on July 24 and 25, respectively. These seeds were taken when the leaves and seed pods were quite dry and the seeds were dark brown and hard in consistency. The relative viability of these four samples of seed are shown in the table below.

TABLE VIII.

SHOWING THE RELATIVE VIABILITY OF SEEDS OF *Hyoscyamus niger* COLLECTED AT VARIOUS STAGES OF MATURITY.

Sample No.	Date of Collection	Percentage of Germination	
		9 Days	18 Days
1	June 21	1.0*	4.0
2	June 25	3.0	6.0
9	July 24	68.0	73.0
10	July 25	93.0	95.0

\* These results are the average of two determinations.

The results presented in Table VIII are very conclusive and show that, in order to secure viable seeds of *Hyoscyamus niger*, they

must be well matured before they are taken from the plant. Seed collected from green plants is practically worthless. The most desirable time to harvest the seeds is when the seed pods and leaves of the plants are becoming dry and the first seed pods are beginning to show signs of springing open.

The hyoscyamus plant, as most all of the members of the night shade family, is a very prolific seed producer. The number of seeds in the pods ranging from 200 to 350, and the number of pods on the larger plants may be as many as 250 to 270.

To determine approximately, the amount of seed that hyoscyamus plants would yield, the mature seed of thirteen representative plants was carefully collected and dried. The seeds of each plant were threshed out by hand and then weighed. The average yields of seed per plant for the thirteen plants under consideration was twenty-three grams.

#### THE ALKALOID CONTENT AND THE UTILIZATION OF THE VARIOUS PARTS OF THE *Hyoscyamus niger* PLANT.

What parts of the plant of *Hyoscyamus niger* can be employed for commercial purposes and at what stage in the growth of the plant is it most desirable to harvest these parts? The U. S. P. requirement for hyoscyamus calls for "the dried leaves and flowering or fruiting tops of *Hyoscyamus niger* (Linné) yielding not less than 0.065 per cent. alkaloid of hyoscyamus." Newcomb and Haynes (8) show results of 0.140 per cent. alkaloid for the flowering tops of the annual variety of *Hyoscyamus niger*, while Carr's (2) work shows 0.12 per cent. of total alkaloid in the dried herb of the first year's growth of this plant. It is true the soil, fertilizer treatment, climate, time of collection and many other factors influence the total alkaloid content of *Hyoscyamus niger*. Since the lowest stated figure is 0.065 per cent. of alkaloid, it is very essential that this amount be contained in the product.

To ascertain the variation in alkaloid content of the leaves of hyoscyamus plants, three average-sized plants were studied. The leaves of these plants were still all green, most of the seed pods had already formed, and just a few small blossoms remained at the upper end of the stem. The leaves and seed pods were carefully taken from each plant and each placed in manila bags and dried. To find out the relation of the alkaloid content of the leaves to that of the

stems and roots, the stems and roots of these three plants were also carefully separated and dried at 60° C.

TABLE IX.

SHOWING THE ALKALOID CONTENT OF THE LEAVES, ROOTS AND STEMS OF  
*Hyoscyamus niger*.

Sample No.	Portion of Plant.	Percentage of Mydriatic Alkaloid.
1	Leaves and seed pods of plant No. 1	0.100
2	Leaves and seed pods of plant No. 2	0.102
3	Leaves and seed pods of plant No. 3	0.073
4	Roots and stems of plants Nos. 1, 2 and 3	0.081

The results as presented in this table show that there is quite a large margin of difference in the alkaloidal content of the leaves and seed pods of sample no. 3 and those of no. 1 and no. 2. But in every case, these figures are well above the U. S. P. requirement. It is interesting to note that the roots and the stems of these three plants taken together have a percentage of 0.081 of mydriatic alkaloid. This figure being a higher amount than the percentage of alkaloid of the leaves and seed pods of plant no. 3. Hence, from this result, we would be justified in utilizing the roots and stems of these plants in conjunction with the leaves.

It is a well established fact that, as the leaves of belladonna plants mature and dry, as the season advances, the percentage of alkaloid therein decreases. To secure more information on this point with regard to *Hyoscyamus niger*, three samples of leaves were collected from hyoscyamus plants, after the seed pods had been removed and the seeds harvested for planting. Similarly, to find the percentage of alkaloid in the dry stems and roots, a series of such samples were collected for analysis.

TABLE X.

SHOWING THE ALKALOID CONTENT OF DRY LEAVES AND STEMS AND ROOTS OF  
PLANTS OF *Hyoscyamus niger*.

Sample No.	Portion of Plant.	Percentage of Mydriatic Alkaloid.
1	Dry leaves taken from six plants	0.057
2	Dry leaves taken from four plants	0.065
3	Dry leaves taken from five plants	0.0619
4	Stems of six plants of sample No. 1	0.052
5	Stems and roots of four plants of sample No. 2	0.0375
6	Stems of five plants of sample No. 3	0.057
7	Roots of five plants of sample No. 3	0.130



On comparing the results as presented in tables nos. 9 and 10, it is apparent that as the leaves, stems and roots mature and become dry, the percentage of alkaloid in these parts is very much less than when these parts are green. While we cannot make an absolute comparison of the results in these two cases as the parts of different plants were employed in the second than in the first case, nevertheless, this difference is so marked that we are quite safe in making the above assertion. It seems quite remarkable that the alkaloid content of the leaves, which were collected after the seed pods had been harvested and the mature seed utilized as such, would be so great, as in no case was the alkaloid content much below the U. S. P. requirement. Upon studying the results of samples nos. 4, 5 and 6, it is seen that these are slightly lower than the results of the analysis of the corresponding leaves of samples nos. 1, 2 and 3, respectively. The sample of roots, no. 7, contained a very high percentage of alkaloids, which would indicate that the roots of *hyoscyamus* can be utilized even after the leaves and stems have matured and dried. Can the leaves, stems, and roots of *Hyoscyamus niger* be utilized for commercial drug purposes when they are dry (have lost all the green coloring matter), and after the seed has matured and has been harvested? If the total mydriatic alkaloid content is a criterion, we would say, that using the above figures as the basis of our information, that it would be impractical to use the dry and dead parts of these plants alone.

#### SUMMARY.

From the data herein presented, we can summarize as follows:

1. If the seed of the annual variety of *Hyoscyamus niger* is viable, 90 per cent. of the viable seed will germinate in from 9 to 11 days.
2. Sterilizing the soil, when using this as a medium in which to test the viability of *hyoscyamus* seeds, increases the percentage of germination 250 to 400 per cent. above the germination produced in unsterile soil.
3. Freezing the moist seeds at  $-12^{\circ}$  C. for four hours, slightly increased the percentage of germination. Treating them with concentrated sulphuric acid did not increase the percentage of germination.
4. Applying a complete fertilizer of 1,000 lbs. of calcium car-

bonate, 800 lbs. of calcium phosphate, 400 lbs. of potassium sulphate, 600 lbs. of sodium nitrate, and 100 lbs. of magnesium sulphate per acre of 2,000,000 lbs., to a clay loam soil, increased the yield of *Hyoscyamus niger*. With this soil, calcium phosphate was the most necessary fertilizer required by this plant.

5. Arsenate of lead (5 lbs. to 100 gal. of water) applied to large plants proved the most effective in controlling the destructive insects, and was not injurious to the leaves. Paris green (1 lb. to 100) destroyed the leaves of these plants. Paris green in dilutions (1 lb. to 150 gal. and 1 lb. to 300 gal.) proved fairly effective in controlling the Colorado potato beetle, but were not as effective as arsenate of lead.

6. *Hyoscyamus* seed for planting should not be collected until the seed pods and leaves of the plant are dry. At this stage, the seeds will be dark brown and the seed coats of a hard consistence.

7. Plants of *Hyoscyamus niger* may easily produce 23 grams of seed.

8. The alkaloid content of green *hyoscyamus* leaves plus seed pods, collected when most of the seed pods had formed, varied in percentage of mydriatic alkaloids from 0.073 to 0.102. The roots plus the stems have a percentage of mydriatic alkaloids of 0.081.

9. Dry leaves of *Hyoscyamus niger*, collected after harvesting the mature seed, had an alkaloid content varying from 0.057 to 0.065 per cent. Hence, the alkaloid content of the leaves when taken from the plants, when mature and dry, is considerably less than those taken from the plants when green. The mydriatic alkaloid content of the stems of the dry plants collected after harvesting the mature seed, was from 0.052 to 0.057 per cent.

10. The stems of *Hyoscyamus niger* collected when the plants are green, can probably always be utilized in conjunction with the leaves and the total alkaloid requirement of the U. S. P. of 0.065 per cent., be met.

Acknowledgment is gratefully made of the valued assistance of Mr. J. R. Butler in the experimental work, and to Mr. George E'We and the analytical department for having made the alkaloid determinations.

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## THE SO-CALLED COLD PROCESS FOR OFFICIAL SOAPS.

BY F. M. JORDAN,

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### LINIMENTUM SAPONIS MOLLIS. TINCTURE OF GREEN SOAP.

The official process involves first the manufacture of the soap, which is later dissolved in alcohol and flavored with oil of lavender. The following cold process completes the preparation in one operation and yields a product which in every way meets the official requirements:



Cotton seed oil .....	279.50 Gm.
Potassium hydroxide .....	55.90 Gm.
Water .....	292.50 mls.
Oil of lavender .....	20.00 mls.
Alcohol a sufficient quantity to make .....	1,000.00 mls.

Dissolve the potassium hydroxide in 180 milliliters of water, and, while still hot, add the cotton seed oil. Add 180 milliliters of alcohol and stir or agitate the mixture until a clear liquid soap results, which should be in about ten minutes. Allow to stand for one hour, add sufficient alcohol to thoroughly liquefy, about 200 milliliters, and 112.50 milliliters of water. Now add the oil of lavender and sufficient alcohol to make the finished product measure 1,000 milliliters. Allow to stand one week and filter.

Assuming that the writer's figures are correct, each ten milliliters of this tincture contain exactly 6.50 Gm. of official green soap. It is now a simple matter to determine the degree of alkalinity using the method directed by the pharmacopœia for standardizing green soap. An excess of alkali must be avoided and the preparation of a test batch of, say 100 milliliters, is suggested. An assay of this test batch gives at once the correct proportion of alkali to oil and the same materials may then be used with confidence for batches of any size.

#### LINIMENTUM SAPONIS. SOAP LINIMENT.

The saponification of olive oil by the cold process is a very simple matter and this fact is perhaps the best argument for the suggested modification of the present official directions. Even a properly and honestly made castile soap, an article by the way which is just now somewhat of a rarity, is by no means easily dissolved in water. The following formula yields a product which in every way meets the official tests for soap liniment:

Olive oil .....	53 Gm.
Sodium hydroxide .....	7 Gm.
Camphor .....	45 Gm.
Oil of rosemary .....	10 mls.
Alcohol .....	700 mls.
Water a sufficient quantity to make .....	1,000 mls.

To the olive oil, contained in a suitable vessel, preferably of

glass, add a solution of the sodium hydroxide in 25 milliliters of water. To this mixture add 25 milliliters of alcohol and agitate the contents of the vessel until saponification is complete and the mass becomes clear, gelatinous and semi-solid. Let stand one hour or longer. Dissolve the camphor and oil of rosemary in 675 milliliters of alcohol, add to the soap just prepared, and, if necessary, add sufficient water to make the finished product measure 1,000 milliliters. Finally mix thoroughly.

#### LIQUOR CRESOLIS COMPOSITUS. COMPOUND SOLUTION OF CRESOL.

The official preparation is a fifty per cent. solution of cresol in a liquid consisting of soap, water and alcohol. The considerable excess of alkali seems unnecessary and the alcohol may be dispensed with as serving no useful purpose. The process below is offered as one in every way satisfactory both from a standpoint of economy in labor and materials and superiority of the finished product. This preparation forms brilliantly clear solutions with water in all proportions.

Cresol .....	500 Gm.
Sodium hydroxide .....	40 Gm.
Linseed oil .....	300 Gm.
Water a sufficient quantity to make .....	1,000 Gm.

To the sodium hydroxide, which must be of full strength, contained in a suitable tared vessel, add 150 milliliters of water and stir until solution has been effected. While still hot, in a thin stream and under constant stirring, add the linseed oil. Continue the stirring until the mass acquires the appearance and consistence of an emulsion and set aside, without further stirring, for twelve hours or over night. To the soap thus formed add the cresol and sufficient water to make the finished product weigh 1,000 grams and stir the mixture until complete solution has been effected, which may be hastened, if desired, by the application of gentle heat. Sodium hydroxide of less than full strength may be used provided its actual strength be taken into account.

## THE HOSPITAL CORPS OF THE NAVY.

NAVAL OFFICERS TELL THE N. P. S. A. ABOUT THE WORK OF  
THE CORPS.

At a meeting of the National Pharmaceutical Service Association held in the Philadelphia College of Pharmacy on Friday evening, December 20, Lieutenant Commander George F. Cottle, Detail Officer of the Hospital Corps of the United States Navy, and Lieutenant W. T. Minnick, Commandant of the Hospital Corps unit, training at the Philadelphia College of Pharmacy, presented a comprehensive and interesting account of the work of the organization in the war.

In the absence of the president, Mr. George M. Beringer, Professor Charles H. LaWall, vice-president, presided. The president was authorized by motion, to publish as a part of the minutes of this meeting a résumé of the work of the Association during the past year and a half, and set forth the need of continued effort by the Association in the interest of recognition of professional pharmaceutical work by governmental authorities.

The facts presented by Lieutenant Commander Cottle and Lieutenant Minnick will prove of great interest to the pharmacists of the country, since they show the important place which pharmacy occupies today in the Navy, and the recognition which it has secured for itself through sheer merit.

Up to 1898 the "apothecary" of the Navy was an appointee of the medical officer under whom he was to serve, being selected from the "baymen" or from civil life. The "baymen" were enlisted men detailed as nurses from other branches of the Naval service and frequently were those who had proven inefficient elsewhere. They were not selected because of special fitness or training for the work. When the services of the apothecary were no longer needed, he was discharged from the Naval service.

As the work of the Medical Corps increased, and more need was found for proper hospital facilities and medical aid, a permanent Hospital Corps was established by law. This was in 1898. The Corps consisted of hospital apprentices, hospital apprentices, first class, hospital stewards, and twenty-five pharmacists, with warrant rank.



No further change was made in the organization of the Corps until 1912, when the rank of "chief pharmacist" was established. This grade carried with it the rank, pay, and allowance of an ensign, which is that of the Annapolis graduate when first detailed to duty.

The services rendered by the Hospital Corps had been of such value as to justify the recommendation by the Surgeon General of the Navy for the advanced rank.

In 1916, in recognition of the efficiency shown by these pharmacists legislation was secured from Congress, authorizing the appointment of as many pharmacists as the needs of the service demanded, and in 1917, the Surgeon General further recognized the importance of the service, by recommending a temporary rank of Lieutenant (Junior grade), and Lieutenant, for 82 of the members of the Corps, and the appointment of 220 Pharmacists (temporary). The several ratings of the Corps are Hospital Apprentices, second and first class; Pharmacist's Mate, third, second and first class; Chief Pharmacist's Mate (acting appointment), Chief Pharmacist's Mate (permanent appointment); Pharmacist and Chief Pharmacist. For the period of the war, all Pharmacists and Chief Pharmacists were advanced first to Lieutenants (Junior grade) and later to Lieutenants, and a large number of Chief Pharmacist's Mates were given temporary appointments as Pharmacists.

The duties of the members of this Corps, especially those who hold the higher ratings, are greatly varied and call for many qualifications and extensive training.

*Nursing.*—Inasmuch as women nurses are not available for sea duty, this group of men are required to perform any nursing duties which the needs of the service may demand, such as the care of the sick, giving of baths, the care of the bed, and bed clothing, taking of temperature, pulse, and respiration, preparing of charts, the administration of enemas and hypodermics, the preparation of patients for the operating room and any of the various services, appertaining to nursing.

*Operating Room.*—In addition to the preparation of the patients for operations, these men are trained to take care of the surgical instruments, and equipment, to do all of the necessary sterilization, know the instruments, care for them and to make all preparation for operations. During the operation, they may serve as assistants to the surgeon, and usually administer the anesthetic. They may

also be called upon to prepare the injection and assist in administering arsphenamine (salvarsan).

*Ward Management.*—The Hospital Corpsmen become the responsible officials, for the establishment and management of the hospitals. They are responsible for the organization of the ward force, for the cleanliness and routine work of the ward, and also responsible for all records and property.

*X-Ray Department.*—A limited number of men have received special training as X-ray operators. This is becoming increasingly important and the complete specialized training must include the knowledge of apparatus and experience in the taking of X-ray pictures and X-ray examinations, and also the development of the plates and making of prints.

*Recruiting.*—In the recruiting stations of the Navy, the hospital corpsmen serve as assistants, making the preliminary physical examinations, preparing the necessary records and securing the identification data, including the making of finger print impressions.

*Commissary.*—Pharmacists are often responsible for the planning of the Commissary department and general equipment of a Naval hospital for any number of patients up to 2,000. This includes not only the equipment of the various wards and divisions of the hospital, but also the procuring of the food, its inspection and the supervision of the preparation of special diets for the patient.

*Transportation.*—The transportation of wounded and sick on board ship is often a difficult problem, and requires knowledge and skill in the methods of handling, the use of stretchers and ambulances, and the preparation of the injured for transportation. This duty falls entirely upon the Hospital Corps.

*First Aid.*—As the hospital corpsman secures experience and rating justifying advancement to the rate of Chief Pharmacist's Mate, he is often placed on "independent duty." Most of the smaller ships of the Navy, destroyers, submarines, mine-sweepers, and cargo ships, need medical aid and the hospital corpsman here serves as the first aid medical officer. Every kind of emergency work may fall to his lot. Sickness, accidents, or other injuries may require his attention at any time. He must be familiar with antidotes to poisons, and all of the many emergency conditions which he may face. This includes, not only the occurrences which may happen aboard ship, but he may be called upon in outlying stations to administer first aid held to the native population.

*Laboratory Technique.*—Their knowledge of chemistry and microscopy must be sufficient to aid in a proper control over the water supply, to make an examination of foods, carry out such clinical tests as may be demanded, such as blood examination, urine tests, examination of feces, the Widal and Wassermann tests, etc., as any of these may become a part of their duty.

*Pharmacy.*—As a pharmacist, the hospital corpsman will have charge of the dispensary either in hospitals on land or on board ship. This rarely calls for the manufacture of pharmaceuticals, but must embrace a knowledge of the medicines on the supply table of the Navy as well as those generally used in medical practice and sufficient chemical training to pass upon the quality of these supplies. The ordering and the proper care of the medical supplies and pharmaceutical equipment, together with the bookkeeping records of the department, the compounding of the prescriptions, and the preparation of such materials as the Dakin-Carrel Solution, are a part of the every-day work.

*Clerical.*—An important function of the hospital corpsman is clerical. The typewriter must be used for reports. They must be familiar with the bookkeeping methods of the commissary department and must be prepared to take charge of or supervise such records. They must supervise the hospital galley (kitchen) and mess-hall, and must oversee the ordering of supplies and are responsible for the storage and quality of foods. They must be familiar with all forms used in the medical corps, and be able to properly prepare them. These forms include records of enlistment, discharge, medical examinations, laboratory tests, sick and death reports, request for leave, official correspondence, etc.

*Hygiene and Sanitation.*—At any time the hospital corpsman may be detailed to serve on shore duty with the marines. Here he occupies the important position of sanitary officer. He must be qualified to establish a camp, look after the water supply, examine the quality of water available, and if necessary, purify it for the troops, take care of all refuse about the camp, establish proper latrines, provide bathing facilities and install and superintend the operation of incinerators for the disposal of all sewerage and refuse. In this service, he must also be prepared to establish and equip a field hospital and superintend its management, as has already been outlined.

This account of the varied duties of hospital corpsmen of the



Navy shows the important place occupied by this branch of the military service. Their work has been so admirably conducted that Naval commanders are now asking for many more men trained in this special branch of the service. The development of the Corps has been slow but it has clearly proven its importance and the need for its existence is being more generally recognized. At the present time, the temporary rank of lieutenant, has been authorized by the Secretary of the Navy and the Surgeon General. The temporary rank of Lieutenant, Medical Corps may not become permanent for the hospital corpsman. This was only a war measure. If those members of the Corps, now holding the temporary rank of lieutenant, were required to pass the examinations for Passed Assistant Surgeon, they would not be able to qualify, since these examinations are for graduates of medical schools. Their work, however, fully justifies the advanced rank they have been given.

The Naval authorities have shown that they recognize the importance of this Corps, through granting these temporary commissions. The Corps has proven its worth, and many members of the Naval Medical Corps and other Naval officers, who have seen the work of the Hospital Corps during the war, are proud of the work it has accomplished. Members of the medical corps of the Army, who have observed Naval Pharmacists at work on transports, have expressed their appreciation of the organization, training and ability.

It will be seen by pharmacists that the duties of members of this corps are far broader than the usual activities of the apothecary in civil life, although pharmaceutical training in accordance with the curriculum of a modern college of pharmacy embraces a large percentage of the work demanded of the hospital corpsmen. The full recognition of pharmacy in the Navy with its related activities, as the collaborator with the physician, in the maintenance of health, treatment of disease, and the healing of wounds, has been established and every pharmacist in the country should lend his aid to the Naval authorities.

Men who secure commissions are required to successfully pass severe competitive examinations. Naval pharmacists firmly believe in proper control over the granting of commissions to Pharmacists in the Navy, and with the new light which has come to all who are interested in the Medical Department of the Navy and in the work of its Pharmacists and Hospital Corpsmen, the N. P. S. A. may well be proud of the work that has been done by pharmacists

in the Naval service and glad of the recognition the Navy has accorded them.

E. FULLERTON COOK,  
*Secretary, N. P. S. A.*

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## PLANTS USED AS INSECTICIDES.<sup>1</sup>

BY R. C. ROARK.

(Continued from page 37.)

ECHINOPS ECHINATUS Roxb. *Compositæ*.

"The roots are pounded and applied to the hair to destroy lice, also the powdered roots applied to wounds in cattle to destroy maggots." (Burkill, quoted by Greshoff, 1913.)

ERIGERON VISCOSUS. *Compositæ*.

In Greece, bunches of this plant are hung over the beds, and all insects that alight upon it are held fast by its sticky exudation. Landerer found that fumigation with it did not narcotize insects as is the case with Caucasian pyrethrum, but did drive them away. (Landerer, Bonplandia, Vol. 10, No. 22, November 15, 1862, p. 342.)

*Erigeron viscosus* is one of the most frequent plants of Greece where it is called psyllorchorton, or flea-plant. Being very viscous before flowering, it is placed in the beds of children to attract the fleas, which adhere to it. The fumes of the burning plant have the same stupefying effect upon the mosquitoes, Sknipes-kenopes (*Culex pipion*) as fumigations of Caucasian insect powder. (Landerer, Am. J. Pharmacy, 4th series, Vol. 5, November, 1875, pp. 498-499.)

EUCALYPTUS GLOBULUS Labill. *Myrtaceæ*. Blue Gum-tree. Victoria and Tasmania.

Leaves = Eucalyptus U. S. P. IX.

Branches of Eucalyptus will drive mosquitoes and other insects out of rooms. (von Mueller.)

EUPATORIUM AMARISSIMUM L. *Compositæ*.

Listed as an insecticide by Greshoff.

<sup>1</sup> Contribution from the Insecticide and Fungicide Laboratory, Miscellaneous Division, Bureau of Chemistry, Department of Agriculture, Washington, D. C.

EUPATORIUM CAPILLIFOLIUM (Lam.) Small. *Compositæ*. Dog-fennel.

It is used to keep off insects and bugs by strewing on the floors of cellars and dairies. (Porcher.)

EUPATORIUM PERFOLIATUM L. *Compositæ*. Synonym: *Eupatorium connatum* Michx. Eastern U. S. Boneset.

The powdered leaves applied to the plant seemed obnoxious to cotton worms (*Alctia*), but the infusion from the leaves was ineffective. (Riley.)

EUPHORBIA BICOLOR. *Euphorbiacæ*.

"The juice of *E. marginata* and *E. bicolor* is used to some extent in Texas to brand cattle, it being held to be superior to a red-hot iron for that purpose, because screw worms will not infect the fresh scar and the spot heals more readily." (Chesnut, U. S. Dept. Agr. Bur. Animal Industry, 15th Ann. Rept., 1898, p. 407.)

EUONYMUS AMERICANUS L. *Celastracæ*. Strawberry Bush. Eastern U. S.

"The seeds are said to be nauseous, purgative and emetic, and are used in some places to destroy vermin in the hair. The leaves are poisonous to cattle." (Porcher.)

EUONYMUS ATROPURPUREUS Jacq. Wahoo. Eastern U. S.

Possesses properties similar to the above. (Porcher.)

EUONYMUS EUROPÆUS L. Spindle-tree. Europe, adv. in U. S.

Seeds emetic, purgative, insecticide. (Lyons.)

FLUGGEEA LEUCOPYRUS. *Euphorbiacæ*.

Leaves used as an insecticide. (Dymock, quoted by Greshoff, Kew. Bull., No. 10, 1909, p. 417.)

GOUANIA DOMINGENSIS L. *Rhamnaceæ*. Chew-stick. West Indies and Brazil.

GOUANIA TOMENTOSA Jacq.

These, and other species of *Gouania*, are used as insecticides. (Greshoff, 1913.)

GYMNOCLADUS DIOICA (L.) Koch. *Casalpinacæ*. Synonyms: *Gymnocladus Canadensis* Lam. (Kew), *Guilandina dioica* L. Kentucky Coffee Tree. Eastern U. S.

Insects preying on the foliage of this tree are poisoned by it. (von Mueller.)



In the south the leaves are used as fly poison. (Pammel.)

The leaves and fruit pulp have been used, when rubbed up with milk, to poison flies. (Chesnut, U. S. Dept. Agr. Div. Bot. Bull. 20, 1898, p. 28.)

HAPLOPHYTON CIMICIDUM A. DC. *Apocynaceæ*.

Arizona to Guatemala and Cuba.

Listed as an insecticide by Greshoff.

HEDEOMA PULEGIOIDES (L.) Pers. *Labiataæ*. Synonyms: *Mellisa pulegioides* L. 1753, *Cunila pulegioides* L. 1762, *Ziziphora pulegioides* Desf. Pennyroyal. Eastern U. S.

No result upon cotton worms (*Aletia*) was observed from the application of the alcoholic extract, decoction or infusion. (Riley.)

Source of the official oil of Pennyroyal; also used to drive away mosquitoes. (Lyons.)

HELENIUM AUTUMNALE L. *Compositæ*.

HELENIUM TENUIFOLIUM Nutt. Sneezeweed. Eastern U. S.

This plant rendered the cotton plant obnoxious to worms (*Aletia*) so that they would not feed upon it, but did not kill them. The decoction, infusion and alcoholic extract were without effect, as were likewise the dried flower heads. (Riley.)

Riley also states: "The universal belief that these two species of dog-fennel are never attacked by any insect is without foundation. We found a small Longicorn borer (larva of *Mecas inornata*) boring in the stem; an unnamed species of *Baris* bores in the root, while the flower-heads are badly infested by several species of *Brachytarsus*."

HELIOTROPIMUM INDICUM L. *Borraginaceæ*. Indian Heliotrope.

The decoction produced no effect upon cotton worms (*Aletia*). (Riley.)

HELLEBORUS ANTIQUORUM A. Braun, ERANTHIS HYEMALIS (L.)

Salisb., HELLEBORUS NIGER L., HELLEBORUS ORIENTALIS, HELLEBORUS VIRIDIS L. *Ranunculaceæ*.

HICORIA GLABRA (Mill.) Brit. *Juglandaceæ*. Synonyms: *Juglans glabra* Mill., *Carya porcina* Nutt., *Hicoria porcina* Raf. Pig-nut, Pig-nut Hickory. Eastern U. S.

An infusion of the leaves in water and washing a horse with

them in fly-time, prevents the annoyance of those insects. (Williams, Trans. Am. Med. Assoc., Vol. 2, 1849, p. 920.)

All the species serve as insecticides. (von Mueller.)

HIPTAGE MADABLOTA Gaertn. *Malpighiaceæ*.

An insecticide. (Greshoff, 1913.)

HYDNOCARPUS ANTHELMINTICA Pierre. *Bixaceæ*.

The seed is used as an insecticide. (Greshoff, 1913.)

INDIGOFERA TINCTORIA L. *Fabaceæ*. Synonym: *Indigofera indica* Lam., not Mill. East Indian Indigo Plant. Tropical countries.

In Jamaica it is employed to destroy vermin. (Porcher.)

The seeds yield a tincture which is used to destroy lice. (Pharmacogr. Ind., quoted by Greshoff.)

INULA PULICARIA L. *Compositæ*.

Flowers of this were entirely inactive against flies. (Kalbruner.)

INULA SQUARROSA (L.) Bernh. Synonym: *Conyza squarrosa* L., *Inula Conyza* DC. Plowman's Spikenard. Europe.

Herb diuretic, emmenagogue, insecticide. (Lyons.)

JUGLANS NIGRA L. *Juglandaceæ*. Black Walnut, American Walnut. Ontario and Eastern U. S.

Walnut leaves soaked in water for some hours, then boiled and applied to the skins of horses and other animals, will prevent their being bitten or worried by flies. (Porcher.)

Riley reports on the action of the alcoholic extract and decoction on cotton worms (*Aletia*) as follows: "A substance which, especially in the form of decoction, deserves further attention. It has no effect on the worms upon contact, but renders the leaves decidedly distasteful to them. On the second day after application the leaves which had received a large amount of the decoction remained fully intact; the worms having removed to the lower branches and to those portions of the plants which were not, or but little, treated with the decoction. Several worms kept in captivity without food except leaves drenched with this decoction finally fed upon them and successfully changed to pupæ. The decoction stains the leaves dark brown, but apparently without injuring them."

JUNIPERUS HORIZONTALIS Moench. *Pinaceæ*. Synonym: *Sabina*

*officinalis* Garcke. Savin. Europe, northern Asia and North America.

A decoction of the tops serves as an insecticide. (Greshoff.)

JUNIPERUS VIRGINIANA L. Red Cedar. Eastern U. S.

The use of red cedar boxes for storing woollens to protect them from moths is well known.

The leaves also prevent the attacks of insects when spread over cloth. (Porcher.)

LEDUM GROENLANDICUM Oeder. *Ericaceæ*. Synonym: *Ledum latifolium* Ait. Labrador Tea. Northern U. S.

It is said to kill lice, insects, etc. (Williams, Trans. Am. Med. Assoc., Vol. 2, 1849, p. 916.)

LEDUM DECUMBENS (Ait.) Lodd. Wild Rosemary. Northern Europe, Asia and North America.

This plant kills lice, bed-bugs, fleas, moths, and other insects. It is most active when green and in blossom, but the dried material is also effective. (Ztschr. allg. oesterreichischen Apotheker-Vereines, Vol. 13, July 20, 1875, p. 346.)

The leaves and twigs are used as an insecticide. (Lyons.)

LINARIA LINARIA (L.) Karst. *Scrophulariaceæ*. Synonyms: *Antirrhinum Linaria* L., *Linaria vulgaris* Mill. Toad Flax. Europe, nat. in U. S.

The expressed juice mixed in milk is a poison to flies, and the smell of the flower also kills them. (Williams, Trans. Am. Med. Assoc., Vol. 2, 1849, p. 917.)

LINUM USITATISSIMUM L. *Linaceæ*. Flax. Europe and Asia, cult. in U. S.

The oil from flaxseed will also destroy all kinds of animals infesting quadrepeds, when rubbed into the skin. (Porcher.)

LYCOPERDON BOVISTA L. *Lycoperdaceæ*. Synonyms: *Lycoperdon giganteum* Batsch., *Bovista giganteum* Nees., *Lycoperdon caelatum* Frice. Giant Puffball.

Used in its mature condition as a styptic and for stupefying bees. (Kew Guide, quoted by Greshoff.)

LYCOPERSICON LYCOPERSICON (L.) Karst. *Solanaceæ*. Synonyms: *Lycopersicon esculentum* Mill. (Kew), *Solanum Lycopersicum* L. *Lycopersicum Solanum*—*Lycopersicum* Hill. Tomato. South America, cult. everywhere.



"Tomato foliage may be placed round fruit trees, like the equally poisonous potato leaves, to prevent the access of insects, and an infusion of the herb serves also as an insecticide for syringing, as first adopted by Mr. Sircy." (von Mueller.)

LYCOPODIUM COMPLANATUM L. *Lycopodiaceæ*. Ground Pine.  
Europe, Asia and North America.

The decoction kills lice. (Williams, Trans. Am. Med. Assoc., Vol. 2, 1849, p. 924.)

LYCOPODIUM SELAGO L. Fir Moss; Tree Moss.

Listed by Greshoff as an insecticide.

LYSIMACHIA NUMMULARIA L. *Primulaceæ*. Creeping Loosetrife.  
Europe, nat. in U. S.

The leaves and flowers, steeped in oil, have the power of destroying insects and worms which infest granaries. (Porcher.)

MACLEYA CORDATA (Willd.) R. Br. *Papaveraceæ*. Synonym: *Bocconia cordata* Willd. Tree Celandine. Japan.

The decoction is used in Japan as an insecticide. (Greshoff.)

MARRUBIUM VULGARE L. *Labiataæ*. Horehound. Europe and Asia,  
nat. in U. S.

In experiments with insecticides on the cotton worm (*Aletia*) Riley reports as follows on horehound: "This decoction emits a very powerful and disagreeable stench, which I could still smell on the cotton plants two days after application, but it had no effect whatever on the worms, nor did it prevent the moths from ovipositing. The alcoholic extract did not possess this unpleasant smell, and had likewise no effect whatever."

MATRICARIA CHAMOMILLA L. *Compositæ*. Synonyms: *Chrysanthemum Chamomilla* Bern., *Chamomilla vulgaris* S. F. Gray, *Chamomilla officinalis* Koch. German Chamomile. Europe and Asia, nat. in U. S.

Flowers = Matricaria U. S. P. IX.

In Portugal it is planted under fruit trees for insecticidal purposes. (von Mueller.)

Flower heads of common chamomile have an action similar to that of genuine Persian insect powder (*Pyrethrum roseum* and *P. carneum*). (Schenck, Canstatt's Jahresbericht, Band V, 1859, p. 11.)

Heads of this exert a similar effect on insects as pyrethrum. (Gieseler, Proc. Am. Pharm. Assoc., Vol. 10, 1862, p. 112.)

Chamomile flowers, if pulverized when dried, and perfectly fresh, have a somewhat similar effect on the oriental cockroach as pyrethrum. (Glover, Rept. U. S. Commissioner Agr., 1874, p. 133.)

Chamomile powder is inert toward roaches. (Hirschsohn, Pharm. Zeitschrift für Russland, Vol. 29, No. 14, April 8, 1890, p. 203.)

MATRICARIA INODORA L.

The flowers have a benumbing effect on flies, acting in 1 to 2 hours. (Kalbruner.)

MATRICARIA MATRICARIOIDES (Less) Porter.

In California *M. Matricarioides* seems to serve similarly medicinal purposes. (von Mueller.)

MELANTHIUM VIRGINICUM L. *Melanthaceæ*. Common Bunchflower. Eastern U. S.

These bunchflowers have long been used to poison flies. (Pammel.)

Root used as a fly poison. (Lyons.)

MELIA AZADIRACHTA L. *Meliaceæ*. *Azadirachta Indica* Juss., *Azadarach deleteria* Medic. Nin Tree. East Indies. Source of Assam or Bangalore gum.

Furniture from its wood is not attacked by insects. (von Mueller.)

MELIA AZEDARACH L. Synonyms: *Azedarach Commelini* Medic., *Azedarach odoratum* Noronha. Pride of India. China to India. Cult. in Florida.

The leaves are insecticidal. (von Mueller and Lyons.)

A poultice of the flowers is said to kill lice. (Watt, quoted by Greshoff.)

Peach trees shaded by this tree are never infested by the aphid. (Porcher.)

The leaves and berries of the Pride of India, packed with dried fruits, will preserve them from insects, and will prevent moths in clothes. . . . The wood is beautifully grained, . . . never being injured by worms. (Porcher.)

A solution or decoction made with the berries of the Pride of India (to a half bushel of the berries put into a barrel add fifteen

gallons of water, and let them soak one or two days) and sprinkled with a water-pot over the plant, will, in most cases, prevent the depredation of the black grub, or cutworm. (Porcher.)

Riley reports tests made by his assistants with this plant as follows:

"I sprayed a decoction of leaves and small twigs on the cotton plants, and I think it had a large effect in preventnig the moths of *Heliothis* and *Aletia* from ovipositing, but it did not destroy the larvæ. The alcoholic extract of the berries and leaves adulterated with twice its quantity of water was sprayed on twelve *Aletia* larvæ, full-grown; most of them fell to the ground, and four died. This experiment was repeated with about the same result; but when the extract was diluted with ten parts of water it failed to bring the worms to the ground." (R. W. Jones.)

"This plant, in the form of alcoholic extracts as well as decoctions, undoubtedly possesses some insecticide properties, acting upon the worms by contact, but in a manner quite different from pyrethrum and kerosene. The acting principle seems to be of a narcotic nature, the worms not showing any unusual disturbance after application. They seem to get benumbed, and, gradually losing their strength, finally loosen their hold and drop to the ground, where they lie without falling in convulsions. The more full-grown worms are, however, but little affected, and of the smaller ones a large proportion recover. This is the most promising plant of the whole number I experimented with, though the extracts and decoctions as applied by myself are altogether too weak to be used as a remedy for the worms. The preparations made from the berries are evidently more effective than those from the leaves. . . . For further experiments I would recommend preparations from the *dried* green berries." (E. A. Schwarz.)

MENTHA PULEGIUM L. *Labiatae*. Synonym: *Pulegium vulgare* Mill. European Pennyroyal, Flea Mint. Europe.  
Serves as an insecticide. (von Mueller.)

MENTHA SPICATA L. Synonyms: *Mentha spicata* var. *viridis* L. 1753, *Mentha viridis* L. 1763 (Kew), *Mentha sylvestris* var. *glabra* Koch. Spearmint. Europe, nat. in U. S. Leaves and tops = *Mentha viridis* U. S. P.



With cotton worms (*Aletia*) no result was obtained with the alcoholic extract of this plant. (Riley.)

MILLETTIA AURICULATA Baker. *Leguminosæ*.

The root is used as an insecticide. (Greshoff, 1913.)

MONARDA PUNCTATA L. *Labiatae*. Horsemint. Eastern U. S.

The alcoholic extract of the leaves was ineffective against cotton worms (*Aletia*). (Riley.)

MYRICA CERIFERA L. *Myricaceæ*.

Maryland to Florida, west to Texas.

The Welsh lay branches of it upon and under their beds to keep off fleas and moths. (Quoted by Porcher.)

NELUMBO LUTEA (Willd.) Pers. *Nelumbonaceæ*. Synonym: *Nelumbium luteum* Willd. American Lotus Lily. Eastern U. S.

According to Schaffner it is said to be used to destroy cockroaches. (Pammel.)

NERIUM OLEANDER L. *Apocynaceæ*. Synonym: *Oleander vulgaris* Medic. Oleander. Mediterranean region.

The bark is very frequently used for the destruction of rats and insects. (Ed. Schaer, *Arzneipflanzen als Fischgifte*, 1897; quoted by Greshoff.)

NICOTIANA TABACUM L. *Solanaceæ*. Tobacco. Tropical America.

The use of tobacco powders and extracts (nicotine) for insecticidal purposes is well known.

PACHYRHIZUS TUBEROSUS Spreng. *Leguminosæ*. Synonym: *Dolichos tuberosus* Lam.

The seeds (in decoction or in the form of powder) are used in Merida (Venezuela) for killing vermin. (Ernst, quoted by Greshoff.)

PADUS VIRGINIANA (L.) Mill. *Rosaceæ*. Synonyms: *Cerasus serotina* Lois, *Prunus virginia* L. Black Cherry. Eastern U. S. Bark = *Prunus Virginiana* U. S. P.

PERSICARIA HYDROPIPER (L.) Opiz. *Polygonaceæ*. Water-pepper. Smartweed. Europe, nat. in U. S.

Neither the decoction nor alcoholic extract of the leaves was effective against cotton worms (*Aletia*). (Riley.)

It is found a convenient and useful application for driving off

flies from wounds, occurring on cattle for instance. (Flora Scotica, p. 207, quoted by Porcher.)

Not infested by caterpillars. (Fernow, quoted by von Mueller.)

PHILADELPHUS CORONARIUS L. *Hydrangeaceæ*. Mock Orange. Europe, cult. in U. S.

This is recommended as an insecticide all over the South, for the only reason, it seems, that it is injurious to stock. Decoction, infusion, and alcoholic extract had no effect whatever on cotton worms (*Aletia*). (Riley.)

PHYSALODES PHYSALODES (L.) Brit. *Solanaceæ*. Synonyms: *Atropa Physalodes* L., *Nicandra Physaloides* (L.) Pers., *Physalodes peruvianum* Kze. Apple of Peru. Peru, cult. and adv. in U. S.

Used as a fly poison in parts of the United States. (Pammel.)

PHYTOLACCA AMERICANA L. *Phytolaccaceæ*. Poke-weed. Ontario and eastern U. S. Root = *Phytolacca* U. S. P.

Dr. Renner, of Maryland, states that the root in either a fresh or dried state is poisonous to cockroaches, and that he and his neighbors have used it with good effect. (Glover, Rept. U. S. Commissioner Agr., 1874, p. 133.)

Riley reports results by his assistants as follows: "Decoction of leaves and berries; also alcoholic extract from the dried root. No result." (R. W. Jones.) "I did not obtain any effect with the decoction prepared by Messrs. Jones and Roane, but a very small quantity prepared by Professor Barnard had a decided effect, killing the young worms and seriously affecting the older ones. It was applied undiluted, by means of a hand atomizer. The extract acted upon contact in a very short time, the young worms falling in convulsions of short duration before dying. The old worms had all recovered the second day. Professor Barnard afterwards told me that this extract was a very strong one." (E. A. Schwartz.)

PICRAENA EXCELSA Lindl. (Kew). Synonyms: *Quassia polygama* Linds., *Picrasma excelsa* Planch, *Simaruba excelsa* DC., *Quassia excelsa* Swz. Jamaica Quassia. West Indies.

The use of quassia wood as an insecticide is well known.

PICPASM AILANTHOIDES Planch. *Simarubaceæ*. Nigaki of Japan.

Decoction of the bark used to kill lice. (Batchelor, quoted by Greshoff.)

PICRASMA QUASSIOIDES Benn. Synonym: *Nima quassioides* Ham.  
Northern India.

Possesses insecticidal properties. (Lyons.)

PIERIS OVALIFOLIA D. Don. *Ericaceæ*. Synonym: *Andromeda ovalifolia* Wall.

A useful insecticide. (Watts, quoted by Greshoff.)

PINUS PALUSTRIS Mill. *Pinaceæ*. Synonym: *Pinus australis* Michx  
Long-leaved Pine. Virginia to Florida and Texas.

Resinous exudate is turpentine, of which Wilson (quoted by Porcher) says: "Turpentine is one of the best means of chasing away fleas whether from place or animal, and a bed of very fine shavings of some wood which abounds in turpentine is one of the easiest and most effectual means of banishing them from dogs."

PODOPHYLLUM PELTATUM L. *Berberidaceæ*. Mandrake, May Apple. Eastern U. S.

No result upon cotton worms (*Aletia*) was observed upon the application of the powdered dried root of this plant, nor upon the application of the powder stirred up in water. (Riley.)

POGOGYNE PARVIFLORA Benth. *Labiataæ*.

"Many of the Indians place the culled plants in or about their houses to drive away flies." (Chesnut, U. S. Dept. Agr. Div. Bot. Contributions from the U. S. Nat. Herbarium, Vol. VII, No. 3, 1902, p. 384.)

PRUNUS SPINOSA L. Sloe; Blackthorn. Europe.

Hardly at all liable to be attacked by insects. (von Mueller.)

PTERIDIUM AQUILINUM (L.) Kuhn. *Polypodiaceæ*. Common Brake.

In Austria the leaves are placed in the bed as a protection against vermin. (Pharmaceutische Zeitung, Vol. 37, No. 103, December 24, 1892, p. 798.)

PULICARIA DYSENTERICA (L.) Gaertn. *Compositæ*. Synonym: *Inula dysenterica* L. Fleawort. Southern Europe.

Herb insecticide. (Lyons.)

PYRETHRUM CALAMITA. *Compositæ*.

Heads of this exert an effect on insects similar to that of Persian insect powder. (Gieseler, Proc. Am. Pharm. Assoc., Vol. 10, 1862, p. 162.)



According to Browne (Rept. U. S. Com. Patents, 1857, Agriculture) Persian insect powder is produced from this species as well as from *P. roseum* and *P. carneum*.

RHINANTHUS CRISTA-GALLI L. *Scrophulariaceæ*. Synonym: *Rhinanthus minor* Ehr. (Kew). Rattle; Rattle-box. Northern Europe, Asia and North America.  
Plant insecticide. (Lyons.)

RHUS CORIARIA L. *Anacardiaceæ*. Tanner's Sumac. Europe.

Carvés records that this plant when in proximity of vines infested by *Phylloxera vastatrix*, destroys this insect. (Sorauer, quoted by von Mueller.)

RICINUS COMMUNIS L. *Euphorbiaceæ*. Synonyms: *Ricinus vulgaris* Mill., *Ricinus medicus* Forsk., *Cataputia minor* Ludw. Castor-oil Plant. Southern Asia.

Castor-oil plants have been found efficacious in freeing rooms from insect life, the leaves of the plant containing a substance which is fatal to flies and other insects. (Chemist & Druggist, Vol. 29, Sept. 25, 1886, p. 410.)

It also helps to drive mosquitoes away. (von Mueller.)

ROSMARINUS OFFICINALIS L. *Labiataæ*. Rosemary. Mediterranean region.

Branches of this shrub will keep off moths from wearing apparel packed away. (von Mueller.)

ROYLEA ELEGANS Wall. *Labiataæ*.

The leaves used as an insecticide. (Greshoff, 1913.)

RUMEX sp. *Polygonaceæ*. Dock Weed.

An alcoholic extract was without effect upon cotton worms (*Aletia*). (Riley.)

RUTA GRAVEOLENS L. *Rutaceæ*. Rue. Southern Europe.

A strong decoction obtained by macerating the leaves of the plant in soap and water, is stated by Forney to be a successful remedy for American blight. (Larbaletrier, Year-Book of Pharmacy, 1902, p. 276.)

SAMADERA INDICA (Gaertn.) *Simarubaceæ*. Synonyms: *Locandi indica* Gaertn., *Samandera pentapetala* C. Don., *Niota pentapetalla* Lam., *Niota Commersoni* Pers.

Hindustan. Bark = Niepa bark; Niota bark.

Listed by Greshoff as an insecticide.

SAMBUCUS CANADENSIS L. *Caprifoliaceæ*. American Elder. U. S.

A decoction made by pouring boiling water over the leaves, flowers or berries of the elder is recommended as a wash for wounds to prevent injury from flies. (Porcher.)

SAMBUCUS NIGRA L. European Elder. Europe.

The leaves of the English elder (*Sambucus nigra*) kill several species of noxious insects. (Porcher.)

"It is said, if fruits are whipped with the green leaves and branches of elder, the insects will not attack them." (M. Cutler, 1785, quoted by Greshoff, 1913.)

SANTOLINA CHAMÆCYPARISSUS L. *Compositæ*. Synonym: *Chamæcyparissus villosa* Mill. Lavender Cotton. Mediterranean region.

Listed by Greshoff (1913) as an insecticide.

SASSAFRAS SASSAFRAS (L.) Karst. *Lauraceæ*. Synonyms: *Laurus Sassafras* L., *Sassafras officinale* Nees, not Sieb., *Laurus variifolius* Salisb. Sassafras; Cinnamon-wood. Eastern U. S. Bark of root = Sassafras U. S. P.

Bedsteads made of it are never infested with bugs. (Porcher.)

Riley found the alcoholic extract from the dried bark of the root ineffective against cotton worms (*Aletia*).

From the root oil of sassafras is obtained, which is an insect repellant.

SAUSSUREA LAPPA C. B. Clarke. *Compositæ*. Synonyms: *Aplo-taxis Lappe* Decaisne, *Aucklandia Costus* Falconer. Costus Root; Cashmere. North Temperate Zone.

The aromatic root of this tall perennial species is of medicinal value. . . . It is said that the annual export has been as much as one thousand tons, a large portion used for incense, further as an insecticide, keeping moths from cloth; the leaves for the same reason being used as emballage for shawls. (De Rinzi, quoted by von Mueller.)

SCHKUHRIA ABROTANOIDES Roth. *Compositæ*. Peru to Argentina.

This annual herb yields locally an insecticidal powder. (von Mueller.)

The flowers of this are used in Peru for the same purpose as insect powder. (Haas, Pharm. Centralhalle für Deutschland, neue folge, Jahrgang V, No. 2, January 10, 1884, p. 19.)

SIDEROXYLON BORBONICUM A. DC *Sapotaceæ*. Synonym: *Sideroxylon Inerme* L.

Listed by Greshoff as an insecticide.

SOLANUM AURICULATIUM Ait. *Solanaceæ*.

A decoction of the berries is used as an insecticide. (Greshoff, 1913.)

SOLANUM CAROLINENSE L., SOLANUM CORNUTUM. Horse Nettle. Eastern U. S.

Riley found the decoction of this ineffective against cotton worms (*Aletia*).

SOPHORA FLAVESCENS Ait. *Leguminosæ*.

A decoction of the stems and leaves is used in Japan as an insecticide. (Greshoff, 1913.)

SOPHORA GRIFFITHII Stocks. Synonym: *Keyserlingia Griffithii* Boiss.

The seed is used powdered and mixed with oil to kill lice in the hair. (Burkill, quoted by Greshoff, 1913.)

SYNANDROSPADIN VERMITOXICUS Engl. *Araceæ*.

The poisonous bulbs serve for the destruction of injurious insects. (Engler, quoted by Greshoff.)

TAGETES GLANDULIFERA Schranck. *Compositæ*. South America.

This vigorous annual plant is said by Dr. Prentice to be pulchrious. (von Mueller.)

TAMUS COMMUNIS L. *Dioscoreaceæ*. Black Briony. Europe.

The powdered root has been recommended to destroy lice in children's heads. (Dujardin Beaumetz, quoted by Greshoff.)

TANACETUM VULGARE L. *Compositæ*. Synonyms: *Chrysanthemum Tanacetum* Karsch, *Pyrethrum Tanacetum* DC. Tansy. Europe and northern Asia, cult. and nat. in U. S.

The flowers of Tansy are also said to have a stupefying effect on insects. (Simmonds, Am. J. Ph., 4th series, Vol. 21, April, 1891, p. 202.)

The alcoholic extract and infusion were without effect on cotton worms (*Aletia*). (Riley.)

An action, similar to that of Persian insect powder is produced by the common tansy, which is sold in the north of England for



similar purposes. (Martindale in discussion of Kirkby's paper, Pharm. J. and Trans., 3d series, Vol. 19, September 22, 1888, p. 241.)

Heads exert a similar effect on insects as pyrethrum. (Gieseler, Proc. Am. Pharm. Assoc., Vol. 10, 1862, p. 112.)

Flowers of this were very feebly benumbing to flies. (Kalbruner.)

TRILISA ODORATISSIMA (Walt.) Cass. *Compositæ*. Synonyms: *Anonymos odoratissimus* Walt., *Liatris odoratissimus* Michx. Wild Vanilla, Vanilla-Leaf. Eastern U. S.

The leaves are used to protect woolen clothes from the attacks of moths. (Jackson, Pharm. J. and Trans., 3d series, Vol. 4, October 25, 1873, p. 322.)

TROPÆOLUM MAJUS L. *Geraniaceæ*. Synonyms: *Cardaminum majus* Moench. Common Nasturtium. Peru, cult. in gardens.

Has some insecticidal value, and it is even said that when planted around apple trees it will rid them finally of the wooly aphis. (von Mueller.)

TYLOPHORA FASCICULATA Ham. *Asclepiadaceæ*.

Leaves and root generally used to destroy rats and other vermin. Proved fatal to man. (Pharmacogr. Ind., quoted by Greshoff.)

UMBELLULARIA CALIFORNICA Nutt. *Lauraceæ*. Synonyms: *Tetranthera californica* H. & Arn., *Oreodaphne californica* Nees., *Linharia californica* B. & H. California Laurel. Calif. to Puget Sound.

"The leaves appear to be very valuable for driving fleas away. One Indian said that they are very effective if strewn about the yard, and one white man assured me that, after spending \$10 to \$15 on flea powders in a vain endeavor to drive these insects away, he had used laurel leaves with very marked success." (Chesnut, U. S. Dept. Agr. Div. Bot. Contributions from the U. S. Nat. Herbarium, Vol. VII, No. 3, 1902, p. 351.)

The tree is never attacked by insects, owing, as it is supposed, to the volatile oil it contains. (Heamy, Am. J. Pharmacy, 4th series, Vol. 5, March, 1875, p. 105.)

VERATRUM ALBUM L. *Melanthaceæ*. Synonyms: *Veratrum album* var. *viridiflorum* Mert. & Koch, *Veratrum Lobelianum* Bernh.,

*Veratrum viride* Roehl. not Ait., N. B. *Veratrum album* Michx. = *V. viride* Ait., *Veratrum album* S. Wats. = *V. californicum* Durande. White Hellebore. Europe and Northern Asia. Rhizome and rootlets = *Veratrum* U. S. P. VIII in part.

The powdered rhizome and rootlets constitute the hellebore used as an insecticide.

VERATRUM VIRIDE Ait. Synonyms: *Veratrum album* var. *viride* Baker, *Veratrum album* Michx. not L., *Melanthium virens* Thunb., *Helonias viride* Ker., not *V. viride* Roehl. American Hellebore. North America.

Rhizome and rootlets = *Veratrum* U. S. P. IX.

Serves like other *Veratrum*s also as an insecticide. (von Mueller.)

VERBASCUM THAPSUS L. *Scrophulariaceæ*. *Thapsus Schraderi* Opiz., *Verabascum Schraderi* G. Meyer. Common Mullein. Europe and Asia, nat. in U. S.

The alcoholic extract and decoction of leaves were ineffective upon cotton worms (*Aletia*). (Riley.)

VERNONIA ANTHELMINTICA Willd. *Compositæ*. East Indies.

Bruised seeds largely employed as a means of destroying pediculi. (Watt, quoted by Greshoff.)

VERNONIA NOVEBORACENSIS (L.) Willd. Synonyms: *Serratula noveboracensis* L., *Behen noveboracensis* Hill. Iron-weed. Eastern U. S.

The alcoholic extract and decoction were ineffective against cotton worms (*Aletia*). (Riley.)

VITEX AGNUS-CASTUS L. *Verbenaceæ*. Chaste-tree. Mediterranean region.

Flies are believed to avoid the tree, so that when they are troublesome, branches are hung in the huts. (Burkill, quoted by Greshoff, 1913.)

WITHANIA SOMNIFERA Dun. *Solanaceæ*.

Used as an insecticide. (Burkill, quoted by Greshoff, 1913.)

XANTHIUM STRUMARIUM L. *Ambrosiaceæ*. Cocklebur. Europe and Asia, nat. in U. S.

No result was obtained with the alcoholic extract and decoction used upon cotton worms (*Aletia*). (Riley.)

XIMENIA AMERICANA L. *Olacaceæ*. Synonyms: *Ximenia inermis* L., *Ximenia spinosa* Salisb. Tallow-nut; Wild Olive. West Indies.

The crushed rind is frequently applied by the negroes in Africa to the sores of domestic animals to keep off the fleas. (Walwitsch, quoted by Greshoff.)

ZANTHOXYLUM CLAVA-HERCULES L. *Rutaceæ*. Synonyms: *Zanthoxylum carolinianum* Lam., *Fagara Clava-herculis* (L.) Small (U. S. P.), *Fagara carolinianum* (Lam.) Engler, *Zanthoxylum fraxinifolium* Walt., not Marsh., *Zanthoxylum tri-carpum* Michx., not Hook. Prickly Ash. Southeastern U. S. The powdered leaves seemed obnoxious to cotton worms (*Aletia*). (Riley.)

The author does not assume responsibility for the statements made relative to the efficacy of the various plants mentioned above, but merely quotes the statements that have been made by various authors. It is probable that further tests of some of the plants will show that many of the statements made relative to their insecticidal action are in error.

This paper is prepared for the purpose of calling to the attention of entomologists promising insecticidal plants for further investigation. Users and manufacturers of insecticides will not be justified in assuming that all of the statements here quoted, relative to the efficacy of the plants mentioned, are in strict accordance with facts.

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## THE SEPARATION AND USES OF CACAO SHELL.<sup>1</sup>

BY A. W. KNAPP, B.Sc., F.I.C.

The regulations recently issued by the Food Controller concerning cacao shell in cocoa have brought this subject again into prominence. Since the famous legal case in 1910 when a cocoa powder containing 18 per cent. of shell was found to be genuine, it has received little attention, and now for the first time in England, the amount of shell that may be present in cocoa has been carefully defined.

<sup>1</sup> Reprinted from the *Journal of the Society of Chemical Industry*, July, 1918.



The quantity of shell produced every year is sufficiently great to make the subject of interest to those who have to consider the scientific use of waste products. By calculation from the official returns on cacao, the world-production of cacao shell is found to be about 36,000 tons per year, of which Europe consumes 22,000 tons. The consumption in Great Britain in 1916 was 4773 tons.

The raw cacao beans of commerce are about the size of almonds and have a thin skin or shell. This averages about 12.5 per cent. by weight; the percentage varies with the size and method of production of the beans. Thus, when the shell has been washed, as in the case of the cacao from Ceylon, it amounts to about 8 per cent., whereas with Trinidad cacao, which is clayed, it varies around 15 per cent.

In the cleaning of the beans a small amount (about 0.2 per cent.) of loose shell fragments is separated. The shell cannot be easily separated from the bean in the raw state, but after roasting, the shell no longer adheres to the bean. It has apparently always been the custom to remove the shell, and to use only the kernels for the preparation of cocoa or chocolate; thus Willoughby in his "*Travels in Spain*" (1664) writes "They first toast the berries to get off the husk," and R. Brookes in his "*Natural History of Chocolate*" (1730) says: "The Indians . . . roast the kernels in earthen pots, then free them from their skins, and afterwards crush and grind them between two stones."

After roasting, both the shell and bean are crisp and brittle, and the small hard radicle, or germ, is loose. All that is necessary to get them in a suitable condition for separation is to crush the bean with as little breaking down to powder as possible, so that the shell is in large solid fragments (nibs). This is frequently accomplished by passing through rolls at such a distance apart that the bean is cracked without being crushed. It may also be effected by using a serrated cone revolving in a serrated conical case. It is usual to pass the broken bean into a germ separator; in these machines use is made of the uniform size and rod-like shape of the germ to effect separation. The germs so obtained naturally contain some nib and fine shell, and this mixture is known as "smalls." The large nib passes on to the husking machine, in which the nib and shell are separated by winnowing in a powerful current of air, the large nib falling through the current, whilst the shell is blown into another compartment. Both nib and shell pass down revolving cylindrical screens,

encountering a larger and larger mesh as they proceed and thus being separated into various sizes. The current of air carries about 0.2 per cent. of the material as dust into a settling chamber. The large shell contains a fair amount of nib and is graded and separated. Starting with 100 parts of raw cacao beans 10½ per cent. of shell is produced. The total "smalls" obtained approach 4 per cent., these "smalls" containing about 36 per cent. of shell. As a result of these separations and the loss which occurs on roasting, only 78.5 per cent. of usable nib is obtained, and this contains about 2 per cent. of shell. Continuous vigilance is required to keep the product up to this standard. The husking machine and shell purifiers occupy a considerable space. Crushing and separating machines to deal with 1 ton an hour occupy 2,200 cubic feet, or roughly to handle 1 lb. of roasted beans per hour requires 1 cubic foot. The space occupied by the "smalls" machine, shell graders, and purifiers would add 50 per cent. We have never heard of any other method of separation of the shell being used.

The price of cacao shell has undergone an extraordinary increase in the last two years. Thus in 1912 the average price was 65s. per ton; in 1913, 1914, and 1915, 70s.; in 1916 it rose to 90s.; in 1917 to 128s.; whilst in May, 1918, it stood at 310s. per ton. The variation in price is even greater than appears from these figures. To appreciate fully the rise we have to deduct the bagging expenses, which are high, shell being a bulky material. Thus the above shell, which is practically free from cocoa, weighs only 9½ lb. per cubic foot (or 32 lb. when ground to powder).

There are other grades of cacao shell from which the manufacturer has not so completely separated the cocoa, and these are more highly priced, *e. g.*,

Grade.	Cacao Nib Present.	Price per ton (Sept., 1916)
1.	less than 1%	120s.
2.	2.8%	130s.
3.	10.0%	150s.
4.	15.0%	200s.

The following are the most representative analyses:

ANALYSES OF CACAO SHELL.

Shell.	Unroasted. Average, Per Cent.	Roasted. Average, Per Cent.	Roasted. Average, Per Cent.	Per Cent.
Water .....	12.51	4.50	4.87	9.30
Fat .....	4.23	4.40	2.77	3.83
Ash .....	10.20	7.30	10.48	8.26
Nitrogen .....	2.19	2.50	2.34	3.00
Fibre .....	16.71	14.00	15.63	13.85
Analyst .....	Zipperer	Booth, Cribb and Richards	Winton, Silver- man and Bailey	Smetham

Cacao shells have long been sold in small quantities in Ireland under the name of "miserables" for the preparation of a table decoction. But it was not till this year that they were sold under fancy names at fancy prices, as much as 2s. per lb. being paid in some cases. Whilst a water extract has, no doubt, a small food value, cacao shell should be regarded as a substance capable of producing an inferior stimulating drink rather than as one giving a food beverage. In this connection reference should be made to a recent paper by J. L. Baker and H. F. E. Hulton on "The Analysis of 'Cocoa Teas.'"<sup>2</sup> Cacao shell contains on an average 1 per cent. of theobromine (the figure given in most published analyses being too low), and this is probably its most valuable constituent when used to prepare a drink. Its proper use is as cattle food; for this purpose until the last six months it was low in price.

Smetham<sup>3</sup> calculated the "food units" as 102, which places cacao shell above maize and meadow hay.

Mr. W. L. Dubois has sent us the following figures, obtained in America, showing the digestible nutrients in 100 lb. of shells: Protein 1.53 lb., fibre 6.45 lb., nitrogen-free extract 40.6 lb., fat 4.91 lb., fuel value 111,079 calories (1 lb. gives 4,404 B.Th.U.). These analytical results have been supported by practical feeding experiments in America, in Germany (see Zipperer), and in Turin by F. Faelli, who obtained an increase in the daily average yield of milk. J. E. Lucas<sup>4</sup> obtained 20 per cent. decrease in amount of milk and 20 per cent increase of fat content. In 1916 it was reported that horses in

<sup>2</sup> *Analyst*, 1918, 43, 189.

<sup>3</sup> J. Lancashire Agric. Soc., 1914.

<sup>4</sup> Bull. Agric. Intell., 1913.



Germany were poisoned by being fed on cacao shells ( $2\frac{1}{4}$  lb. per meal). It was suggested that this was due to the theobromine present in the shell. We feel that this is doubtful, considering that cacao shells have so long been used in compound feeding cakes without complaint. It suggests, however, that it is probably unwise to use a high percentage of it in a diet.<sup>5</sup>

Early in 1915 the transport difficulties were so great that manufacturers of cocoa could not get rid of their shell and hence some thought was given to ways of using it. It has been used as fuel. Its calorific value is a little greater than that of wood (varying from 7,400 to 8,600 B.Th.U.), but being very light it needs careful management. It is most effectively used on a gas plant, the only objection being that the tar which it produces has a nauseating odor. The charred residue can be used as a manure. The shell itself has been used as a manure.<sup>6</sup> In experiments at Bournville it was found to decompose in the ground very slowly, and Mr. J. Lodge recommends that the decomposition should be hastened by placing the shell in a heap, soaking well with water, and turning several times previous to use on the land. Used in this way it gave excellent results both as a manure and as a lightener of heavy soils.

The fat in cacao shell can be extracted by solvents, and as "shell fat" is seen on the market from time to time; this is presumably a regular practice on the Continent. This solvent-extracted fat has an unpleasant taste and an odor like tobacco, which renders it unfit for edible purposes. With theobromine fetching fifty shillings a pound the extraction of the theobromine from shell appears a feasible proposition. We know of no firm actually doing this, although presumably either shell or germ is the source of the theobromine now sold. As an experiment we ourselves extracted some sixty pounds, which we had no difficulty in selling.

Shell can be made to give an extract which is equal to some of the coffee substitutes at present sold, and many other applications have been suggested, but the use of shell which is the most interesting and regrettable is in cocoa and chocolate. In Belgium, Switzerland, Austria, Germany, and America, it is illegal to put shell in cocoa or chocolate, the shelled bean being used. In Great Britain until this year the amount of shell that might be present in cocoa and chocolate had not been defined. The Food Controller has now

<sup>5</sup> See "Cacao Shells as Fodder," by A. W. Knapp, *Tropical Life*, 1916,

issued regulations which state that "no person shall manufacture cocoa powder except such powder as contains no more than 5 per cent of shell." A manufacturer "may sell as Grade A. cocoa powder any cocoa powder which contains not more than 2 per cent. of cocoa bean shell." From the point of view of the public and the manufacturer the figures are well chosen, for when every reasonable effort is made on a commercial scale to separate the shell from the nib, about 2 per cent. of shell is left in. These figures have, however, placed the analyst in a difficult position, for there is no process which will accurately determine such small quantities of shell as 2 per cent. and 5 per cent., and with such processes as are available he will need to draw conclusions from his results with considerable caution. Of the many processes that have been suggested we have most confidence in the fiber determination, but the natural variations in shell and in nib are so great as to make the detection of 5 per cent. of shell uncertain.<sup>7</sup>

In conclusion I wish to thank Mr. N. P. Booth for a number of useful suggestions.

## OCCURRENCE OF MOULD IN COCOA BUTTER.<sup>1</sup>

BY LILY BATTEN AND HUBERT W. BYWATERS.

Cocoa butter is distinguished among fats by its resistance to influences tending to produce rancidity or mouldiness. A case of extensive growth of a mould in a specimen of cocoa butter is therefore interesting and noteworthy. The specimen in question was a large block of butter weighing about 28 lbs., and it had probably been expressed from the cocoa beans several months before it came under our observation. On being broken, it was noted that towards the center of the block, and extending from the upper to the lower surfaces, were a large number of dull black patches, intermingled with streaks of a brownish yellow tinge; the butter had a granular appearance, the whole somewhat resembling a matured Stilton cheese.

<sup>5</sup> See Annual Report of the Experimental Farms in Canada, 1898, 151, and 1899, 851.

<sup>7</sup> See also Baker and Hulton, *Analyst*, 1918, 43, 197-201.

<sup>1</sup> Reprinted from the *Journal of the Society of Chemical Industry*, July, 1918.

An accidental contamination with dirt was at first suspected, but on microscopical examination the dark material was found to consist of innumerable hyphæ of various kinds, and greenish blue conidia of a fungus. It was difficult to identify the individual genera in this mass, so sterile prune-juice agar medium was prepared, poured into Petri dishes, and subsequently inoculated from various parts of the infected material. In this way colonies of the moulds were obtained and *Penicillium glaucum* and pink yeast were found to occur, but the greater part of the original mass was found to consist of a species of *Aspergillus*. A pure culture of the latter was obtained, and it is believed to be *Aspergillus oryzae*. According to Lafar<sup>2</sup> this species is of practical importance as a saccharifying fungus, and has been cultivated for centuries in Japan for the production of saké from rice. It grows rapidly on a large variety of liquid and solid media, and is easily cultivated even at room temperature, the optimum being above 30° C. The peculiarities of the conidiophores, sterigmata, and conidia enable the species to be distinguished with comparative ease from most others, but it is similar to *Aspergillus flavus*, except that in the latter the walls of the hyphæ and conidiophores bear irregular outgrowths. The clavate or spherical globule exhibits no definite line of demarcation from the smooth stem. The sterigmata are radial, and bear numerous large spherical conidia measuring about 0.006 Mm. in diameter.

On breaking open the block of infected butter, drops of clear liquid, apparently water, were observed to be present in some of the larger vesicles. Chemical examination showed the infected part to contain 0.13 per cent. of moisture, and it was thought possible that the spores of the fungi had found their way into the butter by this means. To settle this question, the following investigation of the conditions of growth of *Aspergillus* was carried out: Cocoa butter in sterilized Petri dishes was inoculated from the infected butter, and it was found that the mould would not grow on ordinary cocoa butter at any temperature from room temperature up to 33° C., which is its melting point.

Evidence of the facilitating influence of water on the growth of the mould in the infected block was then sought by preparing a series of sterile Petri dishes, and into them placing (a) ordinary cocoa butter, (b) sterilized cocoa butter, and (c) solidified emulsion of cocoa butter and water (containing about 30 per cent. of water).

<sup>2</sup> *Tech. Mycol.*, 1910, Vol. II., Pt. II., p. 308.



These were then inoculated with the spores of the fungus. In addition, small blocks of the infected butter were placed in contact with blocks of (a) ordinary cocoa butter and (b) solidified emulsion of cocoa butter and water. The dishes were then kept at various temperatures from 15° C. up to 33° C., but at the end of three months in no case could fresh growth of the fungus be observed.

However, colonies of fungoid growth had actually developed on a large block of the solidified emulsion of cocoa butter and water which had been kept at room temperature for the same time, and on reconsideration it appeared probable that the comparatively thin films of cocoa butter and water emulsion in the Petri dishes would rapidly become dry during the incubation, any initial growth of the fungus would soon cease owing to the lack of moisture. This view was corroborated by the fact that in a dish where the block of medium was about as thick as the depth of the dish would allow, growth of the fungus was eventually observed at a temperature of about 27° C. The water content of this butter was 2.4 per cent. which is therefore sufficient to enable the mould to grow.

In all cases growth of the mould appeared to become quiescent after a comparatively short time, although subsequent re-inoculation into a fresh plate was again followed by spasmodic growth. In order to ascertain if the arrest of growth is due to lack of water or another substance, a series of blocks of cocoa butter containing from 0-20 per cent. of water in an emulsified state were prepared, and the fungus introduced into the center of the block, instead of being inoculated into the surface layers. Under these circumstances, however, growth continued to be slow, no matter how large the proportion of water present, but it was rather quicker at 27° C. than at either 12° C. or 17° C.

These experiments seem to indicate that although water is necessary for the growth of the mould, yet the cessation of growth is due to a lack of some other food substance. Although nitrogen could not be detected in the original block by the usual tests, it was thought possible that the addition of a nitrogenous substance might render the cocoa butter more suitable for the propagation of the fungus. Sterile Petri dishes were therefore prepared containing a medium of cocoa butter mixed with a small quantity of sterile prune-juice agar. These were inoculated, and, on incubation at 27° C., vigorous fungal growth was observed in less than a week. Fructifi-

cations were also formed in the following days, with development of characteristic conidia.

These results show that no fear need be entertained of ordinary cocoa butter becoming mouldy from the cause under investigation, provided it is kept free from water. If, however, water finds its way into the cocoa butter—and especially if the water contains substances, probably of a nitrogenous nature, which can serve as food for the fungus—then there is a real danger of the cocoa butter becoming mouldy.

Chemical investigation showed that the acid value of the mouldy butter was about 13, but this was largely due to the presence of the fungoid material, for the acid value of the butter after filtering through paper was only 3.8. This figure, although comparatively low, nevertheless indicates a certain amount of free fatty acid in the butter, and suggests the probability of the appearance of rancidity if the growth of the fungus is unchecked.

The greater part of the experimental portion of this investigation was carried out in the Department of Botany of the University of Bristol.

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## A SIMPLE AND RAPID METHOD FOR THE ESTIMATION OF ALCOHOL IN SPIRITUOUS LIQUORS.<sup>1</sup>

BY NAGENDRA CHANDRA NAG, M.A., F.I.C., AND PANNA LAL, M.Sc.

The method for the estimation of alcohol described below is the result of an investigation to devise a simple method for its estimation with a fair degree of accuracy, avoiding distillation.

The method consists of treating a known quantity of spirituous liquor in a glass tube graduated in tenths of a Cc. (or finer graduation if procurable) with an excess of anhydrous potassium carbonate, adding about 5 to 10 per cent. of water in case the percentage of alcohol is above 90. The mixture is then thoroughly shaken and allowed to settle (or preferably centrifuged), when it will separate into a lower layer of solid potassium carbonate, a middle layer of saturated solution of potassium carbonate, and an upper layer of alcohol hydrate corresponding with the formula  $4C_2H_5OH, H_2O$ , as will appear from the experimental results given below. The

<sup>1</sup> Reprinted from *Jour. of the Soc. of Chemical Industry*, Sept., 1918.

aqueous potassium carbonate solution (middle layer) contains 0.00275 vol. of alcohol hydrate per Cc.

The composition of the alcohol hydrate was determined by density determinations by weighing, as well as by the glass hydrometer at 15.6° C. The results for specific gravity were 0.81961 and 0.8200 respectively, corresponding with 94.04 and 93.92 per cent. of alcohol by volume. The formula  $4C_2H_5OH, H_2O$ , assigned to the hydrate requires 94.061 per cent. of absolute alcohol by vol., 91.089 per cent. by weight. The alcohol hydrate does not leave any solid residue on evaporation, showing that it does not dissolve potassium carbonate. The coefficient of expansion of the alcohol hydrate as determined by a weight thermometer was 0.001076; calculated theoretically by extrapolation from Tralles' Table II. the value 0.001068 was obtained.

The formula obtained for calculating the percentage of alcohol as the results of experiment and on theoretical grounds is as follows: Percentage of alcohol =  $(V + v \times 0.00275) [1 - 0.001068(t - 15.6)] \times 0.7936 \times 94.06 \div W$ , where  $V$  = volume of alcohol hydrate directly read off in graduated tube in Cc.,  $v$  = volume of the saturated potassium carbonate solution (middle layer),  $t$  = temperature observed during the experiment in °C.,  $W$  = weight of the sample taken in Gm., 0.00275 is the solubility (in Cc.) of the alcohol hydrate per Cc. of the saturated potassium carbonate solution, as actually found by experiment, 0.001068 is the apparent coefficient of expansion of the alcohol hydrate, 0.7936 is the specific gravity of absolute alcohol (15.6°/15.6°; it is assumed that the graduation of the glass apparatus used had been carried out at 15.6° C.), and 94.06 is the percentage by volume of absolute alcohol present in the alcohol hydrate liberated (upper layer). (This corresponds to percentage composition by weight, alcohol 91.089, water 8.911, the corresponding density being 0.819514.)

If the volume of saturated potassium carbonate solution is less than 2 Cc. the correction for the solubility of alcohol hydrate in potassium carbonate solution may be dispensed with as it does not appreciably affect the result.

In order further to verify the formula given above, 5 Cc. of Merck's alcohol (marked "absolute alcohol, sp. gr. 0.795") was mixed with saturated potassium carbonate solution, some solid carbonate also being added. The strength of the alcohol as calculated by our formula was 99.46 per cent.; the specific gravity observed



by means of a gravity bottle was 0.79536, corresponding to 99.44 per cent. by weight of alcohol.

The percentage of alcohol found in a sample of whiskey was 39.45 using our method, and 39.47 by distillation (using ice).

Numerous estimations have been made in alcohol solutions and spirituous liquors by this simple method and in many cases the results have been tested and confirmed by hydrometer readings. The results obtained were almost identical by the two methods. The point at which there is some slight disagreement between our experimental figures and those of published tables (Tralles' tables), is where the apparent coefficient of expansion of the alcohol hydrate is 0.001076. This might be urged as additional evidence for the existence of this hydrate.

In conclusion it may be mentioned that the method is quite accurate even though not more than 5 Cc. of the liquor under examination be used. Solids in solution do not affect the result. Loss by evaporation is prevented, as distillation is avoided and readings are taken in closed tubes. Ice is not required even if the temperature be high. This method is equally applicable to methyl alcohol.

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## CREATININ AND CREATIN IN THE BLOOD.<sup>1</sup>

The more recent quantitative microchemical studies of the blood have indicated that among the non-protein nitrogenous constituents the estimation of creatinin is likely to be of especial service from a diagnostic and prognostic standpoint. There are few, if any, normal nitrogenous components of the urine for which the kidneys are more permeable; so that when creatinin begins to accumulate in undue proportions in the circulating blood, there can be little question as to the seriousness of the finding.

But what constitutes an abnormally high content of creatinin in the blood? Folin and Denis placed the normal limits at from 1 to 1.4 Mg. per hundred Cc.; according to Myers and Fine, who have accumulated exceptionally extensive statistics on this question, the range is set at from 1 to 2 Mg. Other investigators have been in essential accord with such figures. Only Gettler and Baker indi-

<sup>1</sup> From *The Journal of the American Medical Association*.

cate 0.5 Mg. as the upper limit of normality; and they have reported many specimens of normal blood to contain as little as 0.1 Mg. The problem of establishing definitely a standard of composition is further complicated by the fact that creatinin has been demonstrated to occur in the corpuscles as well as in the plasma. Obviously only the plasma component can be concerned directly in the passage of creatinin in or out of the circulation. As a recent writer has expressed it, the accumulation of creatinin in the blood has shown itself to be a useful index of renal insufficiency; but we are as yet unaware whether the excess present in the circulation of a nephritic permeates all the elements of the blood, or accumulates in the plasma alone. If the latter alternative should prove to be correct, the variations of the plasma creatinin in kidney disease would be even more striking than those of the whole blood creatinin, and would form a still more delicate index of the organ's capacity to excrete. A separate study of plasma and whole blood creatinin and creatin in different pathologic conditions might even reveal significant variations in the permeability of the corpuscles for these substances.

Thanks to the researches of Wilson and Plass, of the Johns Hopkins Medical School, and more recently of Hunter and Campbell at the University of Toronto, it seems conclusive now that in general the creatinin of normal human blood is distributed among its different elements at a practically uniform concentration. It is not confined more particularly to either plasma or corpuscles. The figures ascertained for the plasma indicate, therefore, also the true creatinin content of whole blood. According to Hunter and Campbell, the creatinin content of normal human blood plasma ranges under different conditions from 0.7 to 1.3 Mg. per hundred Cc., the average for sixty specimens examined being 1 Mg. This is in substantial agreement with the figures of all the previous workers except Gettler, whose divergent results were reported above.

With respect to the content of creatin in the blood, the conditions are apparently unlike the equal distribution of creatinin. Hunter and Campbell believe that the creatin is chiefly concentrated in the corpuscles. With the method used, exact determinations were unattainable; but it is roughly estimated that the average creatin content of the corpuscles lies between 6 and 9 Mg. per hundred Cc., while that of the plasma is not more than from 0.4 to 0.6. The blood as a whole contains apparently an average of about 3 Mg. per hundred Cc. There seems to be more in the blood of females than

of males. In other words, the corpuscles contain from five and a half to ten times as much creatin as creatinin, while in the plasma it is the latter that is predominant.

The Toronto investigators point out that the blood creatinin is apt to be lower in females than in males, and lower in subjects deprived of exercise than in those leading an active life. It is suggested that the blood creatinin is related to muscular development in much the same way as the creatinin coefficient of the urine. We have already discussed the peculiar occurrence and as yet unknown significance of creatin in the urine. Hunter and Campbell have found this substance present at times in the blood. They state that there is a distinct correspondence between increase of plasma creatin and the appearance of creatin in the urine; but whether the plasma, in the absence of creatinuria, is creatin-free or whether there exists a threshold for creatin excretion has not been positively determined. If there is a threshold, it is a very low one.

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## CURRENT LITERATURE.

### SCIENTIFIC AND TECHNICAL ABSTRACTS.

A RAPID TEST FOR OCCULT BLOOD.—The benzidine test for occult blood was referred to in these pages (1916, p. 249), when the method of application was described as follows:

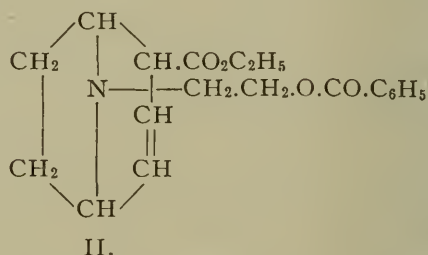
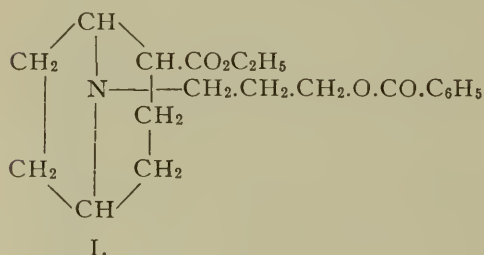
To about 5 Cc. of a saturated solution of benzidine in alcohol or glacial acetic acid an equal volume of 3 per cent. hydrogen peroxide solution is added, and then one Cc. of the solution to be tested. If the mixture is not acid, it is made acid with acetic acid. A green or blue color indicates the presence of blood. A control test in which water is substituted for the liquid under examination should give no coloration. The test is said to detect blood in a dilution of one in 300,000.

W. T. Vaughan (*Jour. Lab. and Clin. Med.*, 1917, 2, 437, Mar.) gives a simple modification of this test which can be applied by any physician. A few grains of powdered benzidine (as much as will lie on a knife-point), with a few drops of glacial acetic acid and a few drops of hydrogen peroxide, are mixed with a small portion of solid fæces on a glass slide: a greenish-blue fading color is positive. This test, he concludes, is simple, rapid and clean, and is not



too delicate for clinical use. (Reprinted from *The Prescriber*, August, 1918.)

CONVERSION OF COCAINE INTO NEW, PHYSIOLOGICALLY SUBSTANCES.—By a chemical procedure the functional elements of cocaine are rearranged to yield two new active substances: (I) "Mydriasin," as strong a mydriatic and anæsthetic as atropine, chemically



benzoyloxypropylnorhydroecgonidine ester; and (II) "Ekkain," a stronger anæsthetic than cocaine, non-toxic, and sterilizable. Chemically it is N-benzoyloxypropylnorecgonidine ester. It is an oily compound whose hydrochloride melts at 117° and is easily soluble in water, less so in alcohol. (J. v. Braun and E. Müller, *Ber. d. d. chem. Ges.*, v. 51, pp. 235-252, 1918.)

J. F. C.

THE CASEIN OF HUMAN MILK.—Analysis of the casein of human milk yielded the following figures: Nitrogen, 15.75 per cent.; phosphorus, 0.70 per cent.; sulphur, 0.70 per cent. From its combination with bases the molecular weight was calculated to be 8,888 and its valence 8. It was found to resemble the casein from the milk of the cow and of the goat. Rennin produces a paracasein from it similar to the paracasein from cow's milk. (A. W. Bosworth and Louise A. Giblin, *Jour. Biol. Chem.*, v. 35, pp. 115-117, 1918.)

J. F. C.

THE PREPARATION OF PURE CASEIN.—Casein in pure form, free from inorganic phosphorus, calcium, and hydrolytic products, is prepared by treating undiluted milk with normal acid, preferably lactic or a mixture of 1 part of hydrochloric and 2 parts acetic. The acid is introduced slowly into the undiluted milk below the surface, the tip of the tube carrying the acid into the milk being so arranged that it is very close to a mechanical stirrer revolving at high speed and

also near the bottom of the vessel containing the milk. Under these conditions the acid does not cause coagulation of the casein at the point where the acid first comes into contact with a portion of the milk. The ash and phosphorus contents of this casein are unusually low. Casein can be prepared by this method within ten hours; excess of acid and danger of hydrolysis are avoided; the product contains neither inorganic phosphorus nor calcium; it is quickly soluble in dilute alkalies; the yield is practically quantitative. (L. L. Van Slyke and J. C. Baker, *Jour. Biol. Chem.*, v. 35, pp. 127-136, 1918.)  
J. F. C.

ORGANIC CRYSTALLINE SUBSTANCES IN GENTIANA GERMANICA.—Two crystalline substances were detected: gentiolutein, a sublimate of yellow needles which is insoluble in water, alcohol, glycerol, aqueous chloral hydrate, olive oil, dilute mineral acids, but is easily soluble in acetone; and a second substance observed after the removal of the epidermis of the leaf and immersion in distilled water or treatment with dilute mineral acids or phenol, alcohol, or glycerol. Neither substance is identical with gentiopicrin or gentianin. The gentiolutein could not be detected in *G. asclepiadea*, *G. ciliata*, or *G. pneumonanthe*. (Hans Molisch, *Ber. botan. Ges.*, 35, 653, 1917; *C. A.*, 12, 2344, 1918.)  
J. F. C.

THE EFFECTS OF VARIOUS AGENTS ON SUPERFICIAL HEMORRHAGE AND THE EFFICIENCY OF LOCAL HEMOSTATICS.—Beginning with the most efficient, the order of efficiency of the more important of all the hemostatic agents tested is epinephrin, pituitary extract, tyramin, acetic acid, ferric chloride, quinine-urea-hydrochloride, tannin, sodium bicarbonate, barium chloride, cane sugar, sodium chloride. A number of other agents, which were tried, can lessen local hemorrhage in variable degrees, but on the whole they are inferior and undesirable for various reasons. The following among the more important of this class and for which hemostatic claims have been made, were found to increase bleeding on local application; cotarnine salts (stypticin and styptol), antipyrin, pepton<sup>e</sup>, emetine, sometimes alum, orthoform (1 per cent. solution) also quite markedly increased local bleeding. Under the conditions kephalin, coagulen, and thromboplastin were all variable, or did not affect the course of

bleeding. (P. J. Hanzlik, *Jour. Pharmacol. and Exp. Ther.*, v. 12, pp. 71-117, 1918.)

J. F. C.

THE EFFECTS OF VARIOUS SYSTEMIC AGENTS ON SUPERFICIAL HEMORRHAGE.—The most effective hemostatic agent on superficial bleeding by systemic (intravenous) administration was epinephrin; tyramin somewhat less; pituitary extract was variable. Fatal doses of ergot and digitalis (one experiment each) also lessened and arrested, respectively, the bleeding. The effects of the following (systemically) on bleeding are roughly parallel to the changes in blood pressure: coagulen (Ciba), kephalin (Howell), thromboplastin (Squibb), horse serum, stypticin, gelatin, saline, emetine, and possibly peptone. Nitrite and hydrastis increased bleeding with a fall in pressure. The results with the thromboplastic agents might be different with prolonged administration. (P. J. Hanzlik, *Jour. Pharmacol. and Exp. Ther.*, v. 12, pp. 119-128, 1918.)

J. F. C.

ATOPHAN AND SEVERAL OF ITS DERIVATIVES.—Atophan is toxic to cold-blooded but not to warm-blooded animals; it paralyzes the central nervous system and the nerves of the heart in frogs. After administration to men the uric acid excretion was much increased, the atophan being excreted as hydroxyphenylquinolinecarboxylic acid which will, itself, increase uric acid excretion. (L. Rotter, *Z. exp. Path. Ther.*, 19, 176, 1918; *C. A.*, 12, 2384, 1918.)

J. F. C.

## MEDICAL AND PHARMACEUTICAL NOTES.

STANNOXYL IN STAPHYLOCOCCAL INFECTIONS.—In *The Prescriber*, June, p. 111, reference was made to the experience of A. Compton in the use of stannoxyl (a mixture of tin and tin oxide) as a remedy for the mixed infection of pulmonary tuberculosis. The dose was there given as one Gm. daily. In a later communication (*Lancet*, 1918, 2, 234, Aug. 24) the same author reports on the use of this substance in three cases of broncho-pneumonia. The dose given was four one-Gm. tablets the first day, six the second, and eight per day afterwards. The pulse and temperature dropped; night sweats diminished; the sputum became less, and the weight gradually increased. (*The Prescriber*, October, 1918.)



DICHLORAMINE-T: POINTS IN USE.—Walter E. Lee (*Annals of Surgery*, 1918, 67, 14, Jan.) calls attention to certain points to be observed in handling dichloramine-T or its solutions. All bottles should be of dark amber, glass-stoppered. They should be thoroughly cleaned and dried before any of the materials are put in. If alcohol is used for drying the bottles, it should be allowed to evaporate completely before the bottles are used; no solutions should be returned to the stock bottles from the ward bottles or atomizers at any time; bottles in which the solution has already undergone decomposition should be carefully cleaned with hot water, and dried thoroughly. If, in using the 20 per cent. solution, medicine droppers or glass rods are used to transfer the oil to the wound surfaces, the droppers should be dry if put into the oil bottles. The common practice in some places has been to boil these utensils to sterilize, and then use them while still wet. This results in the gradual accumulation of water in the stock bottles, and a very rapid decomposition of the dichloramine-T. The glass rods or pipettes or syringes if left in contact with the oil for five or ten minutes are entirely sterilized, and do not need boiling. The method the authors have followed is to pour the required amount for the wound into a clean dry medicine glass, and to take the oil with the pipette from the second container. (*The Prescriber*, October, 1918.)

TRINITROTOLUENE POISONING.—A. W. Gregorson and F. E. Taylor place on record five cases of "TNT" poisoning, two of which were fatal. Gastric disturbances and peripheral neuritis were the earliest symptoms, headache, anæmia, and jaundice following in the order named. The intensity of the jaundice varied from week to week, and it was noticed that as the color faded the patients showed signs of improvement. The treatment recommended is as follows: Absolute rest in bed and warmth are essential. *Diet*—Milk, with 5 grains sod. bicarb. to the ounce; 6 ounces to be given two hours. Tea or coffee, *ad lib.* Benger's food, milk pudding, virol, imperial drink, barley water, albumin water, fish, rabbit, vegetables, but all excess must be carefully avoided, and fatty and saccharine foods prohibited. There must be a free exhibition of alkaline beverages to counteract the tendency to acid intoxication. *Medicines*—Calomel, 2 grains, followed by saline eight hours later; and the bowels regulated with cascara sagrada and sodium sulphate. To correct intestinal acidity it is

best to prescribe an insoluble alkaline carbonate such as magnesia. A mixture containing potassium citrate, sodium bicarbonate, and sodium sulphate should be given every four hours. Later, the patient may be given a mixture containing potass. bicarb., tinct. zingib., tinct. rhei co., and infus. gent. Rectal salines, with sod. bicarb. 2 ounces to the pint, may be given every six hours. Intravenous or subcutaneous saline injection, when the patient is first seen, gives great relief, and inhalation of oxygen through warm ether is a valuable stimulant. (*Glasgow Med. Jour.*, 1918, 2, 65; Aug. *The Prescriber*, October, 1918.)

COPPER SULPHOCARBOLATE.—The salts of copper have never been held in much favor as medicinal agents, particularly for internal use. Recently, however, a wave of enthusiasm has spread regarding copper preparations, and numerous investigators have reported on the use of copper compounds in cancer and in tuberculosis. In these cases the preparation recommended has been either a colloidal form of the metal or some special organic compound. Several reports have come from different quarters regarding one of the salts of copper—the sulphocarbolate. As these reports appear to be reasonable and well vouched for, a brief description of its properties and uses may be of interest.

Copper sulphocarbolate,  $\text{Cu}(\text{C}_6\text{H}_4\text{OH}\cdot\text{SO}_3)_2$ , occurs in greenish crystals, and is fairly soluble in water. The dose ranges from  $\frac{1}{128}$  to  $\frac{1}{24}$  grain. Like other inorganic salts of the same metal, large doses act as emetic, but in the doses mentioned no irritant action need be feared. Its action is that of an antiseptic, and it is particularly indicated in various forms of diarrhoea, especially when this is of a choleraic character. In an article in *The Prescriber* (1913, p. 176) its action as an intestinal antiseptic was fully described. The dose recommended is  $\frac{1}{24}$  grain every hour: one grain in three ounces of water, a teaspoonful every hour. G. L. Servoss speaks highly of its uses in cases of food fermentation in children. In the preparation of food for bottle-fed babies he advises the addition to the water of a minute dose of copper sulphocarbolate. In addition to its antifermentative action, it admits of the water being used unboiled, and therefore containing all the original lime salts, an important consideration in the case of children. In the digestive disturbances common to children teething its action is also very

useful. A reference to its use in choleraic diarrhœa in India appeared in *The Prescriber*, June, p. 111.

The suggestion has also been made that it may be used in typhoid fever, but few authentic cases have been recorded of its employment in this disease. From the fact that a minute trace of copper has been found to kill the *Bacillus typhosus* in an hour, it would appear reasonable to try the salt. (*The Prescriber*, August, 1918.)

THERAPEUTIC ACTION OF "BENZOL."—The frequent references in current medical literature to the use of "benzol" in leukæmia make it desirable to have definite information as to the actual substance that is referred to. Benzol (B. P., 1898) is not suitable for medicinal use, and the substance referred to in this connection is what is more correctly known as *Benzene*, or crystallizable benzol, now official as *benzenum* (B. P., 1914),  $C_6H_6$ . This is a hydrocarbon obtained by the fractional distillation of coal tar, and is a colorless, mobile liquid, sp. gr. 0.880 to 0.887. When cooled to  $0^\circ$  C. it solidifies. The benzol of the 1898 Pharmacopœia is a mixture of hydrocarbons, and is suitable only for cleaning purposes or as a solvent.

The action of medicinal benzene is described in the list of new and non-official remedies published by the American Medical Association, from which the following extract is taken:

"When swallowed, this drug usually produces a sensation of burning in the stomach. Benzene is a narcotic which, when swallowed or inhaled, produces vertigo, delirium, and tonic convulsions, followed by deep sleep; 30 Cc. (one ounce) of nearly pure benzene has proved fatal. In some cases the chronic poisoning petechial spots, due to small hemorrhages, have been observed. These spots have been attributed to fatty degeneration of the blood vessels. It produces leucocytosis followed by leucopenia, with an occasional increased number of erythrocytes. Larger doses may produce an aplastic anæmia. Benzene has been used occasionally on account of its narcotic properties, and has also been used as an intestinal antiseptic. It is, however, rarely used for these purposes at the present time. It has been somewhat extensively used in the treatment of leukæmia. Moderate doses cause a rapid destruction of leucocytes, especially the lymphocytes. This action is accompanied by an improvement in the subjective symptoms, and, in some cases, by a marked reduction in the size of the spleen. In many cases



the lymphocytes have been reduced to the normal figure. In others the number of leucocytes has still remained high, although the size of the spleen was reduced. In many cases the improvement is such that an apparent cure is produced. However, a large number, if not all, of these patients relapse or succumb to the toxic action of the benzene. It is recommended to stop the administration of this drug before the leucocytes are reduced to the normal level. Benzene has also been used in a few cases of Hodgkin's disease and in cases of polycythemia. The effect of benzene on the leucocytes is largely enhanced by the previous or simultaneous treatment by the x-ray. The value of benzene in leukæmia is not established, and caution against too large and too long continued dosage should govern its employment.

"*Dosage*.—0.5 to 1 Cc. (8 to 15 minims) given four times a day. Medicinal benzene may be given in capsules or in an emulsion, or may be administered by rectum. Frequent examinations of the blood should be made during the administration of medicinal benzene to determine when it is advisable to suspend the administration of the medicine." (*The Prescriber*, August, 1918.)

"X. Y. Z." PASTE.—Under this name the following paste is recommended by A. E. Morison (*B. M. J.*, 1918, 1, 343, Mar. 23) as an alternative to "BIPP" in the treatment of certain classes of wounds:

Xeroform (bismuth tribromphenol).

Ammoniated mercury .....Equal parts

Liquid paraffin .....Sufficient to make paste.

(*The Prescriber*, August, 1918.)

MAGNESIUM SULPHATE SOLUTION.—The following is the solution recommended by Morison and Tulloch for wound treatment:

Magnesium sulphate ..... 40 ounces.

Glycerin ..... 10 ounces.

Water, boiling .....to make 80 fluid ounces.

MAGNESIUM SULPHATE CREAM.—

Magnesium sulphate ..... 1½ lbs.

Glycerin of carbolic acid (1:10) ..... 11 ounces.

Mix by trituration in a warm mortar. This cream is very hygroscopic, and must be preserved in covered jars.—Morison (*B. M. J.*, 1918, 1, 342, Mar. 23). (*The Prescriber*, August, 1918.)

EUSOL.—J. L. Smith (*B. M. J.*, 1917, 2, 386, Sept. 22) gives the following simple method for the preparation of eusol:

Liq. calcis chlorinat., B.P. ....	135 Cc.
Boric acid solution (4 per cent.) .....	250 Cc.
Water .....	to 1,000 Cc.

Dilute the chlorinated lime solution with water to 750 Cc., and add the boric acid solution. Should the solution be required for intravenous injection, dissolve 8.5 gm. of sodium chloride in 250 Cc. of water, and use this in diluting the chlorinated lime solution. (*The Prescriber*, August, 1918.)

METALLIC TIN AND STANNIC OXIDE AS A REMEDY FOR BOILS.—It has been noticed that among the tin workers in Beauce furunculosis is unknown, and metallic tin, or tin oxide, is regarded by them as a certain cure for boils. The authors have proved that both the metal and its oxide have decided bactericidal action. They found also that when administered to dogs for twenty consecutive days in daily doses of 2 Gms. no ill effects were evident, although the metal was absorbed, and could be detected in the urine for sometime after administration had ceased. They then proceeded to treat fifty cases of furunculosis with doses of 50 Cgms. to 1 Gm. of powdered tin, or its oxide. The results obtained have been excellent. The boils disappeared in five to fourteen days, and there were no relapses. (Frquin and Grégoire *Comptes rend.*, 164, 794, through *The Pharm. Jour. & Pharm.*, August, 1918.)

CURING WARTS BY SOLAR RAYS.—The following simple method is claimed to radically cure warts. The sun's rays are directed by means of a lens into a focus of small diameter on the wart. If the heat is greater than can be borne, the height of the lens is altered and the irradiated spot widened. In either case, in bright sunshine, 30 seconds exposure is sufficient for each wart. In four or five days after this treatment the superficial portions of the wart will be browned and mortified. These are removed carefully with a sharp knife or razor, and the fresh surface is again exposed to the sun bath under the lens. Generally this second treatment will be sufficient, and the wart will shrivel up and fall off after a few days. If it does not the treatment may be repeated. (Dr. Vallet *Presse Méd.: Répertoire de Pharm.*, 1917, 28, 244, through *The Pharm. Jour. and Pharm.*, August, 1918.)

IODIDE OF STARCH AS AN ANTISEPTIC FOR WOUNDS.—Iodide of starch is recommended as an antiseptic for dressing wounds. It is very active as a bactericide, is stable, is not immediately destroyed by contact with the tissues, and may be left in contact with the wound for many hours, or even for several days, if necessary. Ordinary iodide of starch containing 18 to 20 per cent. of iodine is too irritant for this purpose. A combination of 1 part of iodine with 99 parts of starch is sufficiently active and is free from any irritant action. This is applied direct to the surface in powder form, or as a gelatinous paste by warming it with water. Usually wounds are found to be free from organisms after the third dressing with this. If it is desired to use Carrel's irrigation method, the following solution may be used. Soluble starch 25 Gms.; solution of iodine and potassium iodide, 1:100, 50 mls; boiling water to make 1,000 mls. This contains 0.5 Gm. of iodine in 1 liter, and has an antiseptic power similar to that of Dakin's solution. It is non-irritant, and the adjoining surfaces need not be protected from its action. It has no destructive action on textile fabric, which the hypochlorites rapidly attack. (A. Lumière, *Comptes rend.*, 1917, 165, 376, through *The Pharm. Jour. and Pharm.*, August, 1918.)

ATOPHAN AND SEVERAL OF ITS DERIVATIVES.—Atophan is toxic to cold-blooded but not to warm-blooded animals; it paralyzes the central nervous system and the nerves of the heart in frogs. After administration to men the uric acid excretion was much increased, the atophan being excreted as hydroxyphenylquinolinecarboxylic acid which will, itself, increase uric acid excretion. (L. Rotter, *Z. exp. Path. Ther.*, 19, 176, 1918; *C. A.*, 12, 2384, 1918.)

J. F. C.

THE EFFECT OF VARIOUS AGENTS ON SUPERFICIAL HEMORRHAGE AND THE EFFICIENCY OF LOCAL HEMOSTATICS.—Beginning with the most efficient, the order of efficiency of the more important of all the hemostatic agents tested is epinephrin, pituitary extract, tyramin, acetic acid, ferric chloride, quinine-urea-hydrochloride, tannin, sodium bicarbonate, barium chloride, cane sugar, sodium chloride. A number of other agents, which were tried, can lessen local hemorrhage in variable degrees, but on the whole they are inferior and undesirable for various reasons. The following among the more important of this class and for which hemostatic claims have been



made, were found to increase bleeding on local application; cotarine salts (stypticin and styptol), antipyrin, peptone, emetine, sometimes alum, orthoform (1 per cent. solution) also quite markedly increased local bleeding. Under the conditions kephalin, coagulen, and thromboplastin were all variable, or did not affect the course of bleeding. (P. J. Hanzlik, *Jour. Pharmacol. and Exp. Ther.*, v. 12, pp. 71-117, 1918.)

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J. F. C.

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## BOOK REVIEWS.

ANNALS OF THE MISSOURI BOTANICAL GARDEN, No. 3, Vol. v, September, 1918.

Three articles of general botanic interest appear in this number of the *Annals*. The first of these is by E. A. Burt, mycologist to the Missouri Botanical Garden, and is entitled "The Thelephoraceae of North America." The author discusses the structure and distribution of fourteen species belonging to the genus *Aleurodiscus* that occur in North America. Accompanying the description of each species are valuable sketches of diagnostic portions of the fructifications. A key to the identification of the species is also given.

The second article is on "A New Selaginella from Mexico," by J. M. Greenman and Norma E. Pfeiffer. This species was collected with other plants in southern Mexico by Dr. W. J. G. Land and Prof.

Chas. R. Barnes in 1908, and has been named *Selaginella Landii* by the authors, after one of the collectors. Its characteristics are set forth both in Latin and English and by two splendid plates which portray both its habit and morphological peculiarities.

In the third article, entitled "A Wood-penetrating Alga, *Gomontia Lignicola*, nov. sp.," George T. Moore records his observations on a new species of *Gomontia* which he found growing within the tissues of yellow-pine wood, submerged in a fresh-water pond on Nashawena, Elizabeth Islands, Massachusetts. The author has carefully worked out the entire life history of the species which is here for the first time described and clearly illustrated by 19 figures on 3 plates.

HEBER W. YOUNGKEN.

AMERICAN METHODS IN FOREIGN TRADE, by George C. Vedder, First Edition. Published by McGraw-Hill Book Co., Inc., New York, N. Y., 204 pp.

This work is an admirable statement of the general principles that should obtain in the prosecution of American export trade. Not only is it a keen analysis of trade conditions, but its many valuable suggestions are evidently those of a practical man with a wide and fruitful experience.

Mr. Vedder states: "American manufacturers are not the best exporters in the world, but the best exporters in the world are American manufacturers. Volume of sales is not an all important consideration for it takes care of itself in due time if the methods are sound and constructive and possess continuity. Our weakness in the foreign trade field is not that we do not know how to export, but rather that, as yet, good American exporters are relatively few in number. The reality of the existence of distinctively American methods of building up a foreign trade may come as a surprise to many of our manufacturers, into whose ears has for two decades been pouring a crescendo stream of adverse criticism of their handling of export business. Our successful exporters have not imitated the English, French and German traders, but have studied their markets for themselves and solved the problems by the application of good business principles as they knew them. They have followed the Golden Rule in their dealings with buyers in overseas markets."

One of the most striking chapters is that on "The Fundamental Weakness of the German Trade Policy," which says in part:

"German business principles and methods were as much the offspring of autocracy as were the governmental policies of that country. Just as the naval and military establishments of the Kaiser disregarded all laws of civilization and humanity in the prosecution of their war aims, so German industry, supervised and directed, not by independent individuals whose survival depended on their fitness to serve society, but by imperial authority whose favor or disfavor decided to a large extent the average citizen's future, broke most of the basic laws, of good business and fair competition as we understand them."

Contrast the German standard with that of the American manufacturer, with his fine idealism, as thus portrayed by Vedder:

"The ideal exporting manufacturer is one who regards himself, not as a divinely appointed purveyor to the needs of other less able men, but as the privileged director of facilities of production that are necessary to society's welfare. He thinks not so much of his rights as his blessings, not so much of his talents themselves as of what they can do for the world, humbly acknowledging that the qualities of mind that make him a leader are largely unearned blessings and not a reason for deserved self-congratulations."

It is not possible to here detail the many interesting features of this work, such as nationalization of foreign trade, combination in foreign trade, export commission house, selling agent, manager, and manufacturer, exportation of raw, staple and standardized products, publicity, salesmanship, credit, correspondence, banks, investments, treaties, international crooks, tariffs, the "Made in Germany" idea, German competition, etc., but every phase of these questions is fully and most ably discussed.

To the American manufacturer who wishes to do export trade this book is indispensable.

J. W. ENGLAND.

#### REPORT OF THE PUBLIC HEALTH SERVICE.

The Annual Report of the Surgeon-General of the Public Health Service of the United States for the fiscal year ending June 30, 1918, has just appeared. This is the forty-seventh annual report covering the one hundred and twentieth year of the Service's existence.

By order of President Wilson, July 1, 1918, declaring that "All



sanitary or public health activities carried on by any executive bureau agency or office, especially created for or concerned in the prosecution of the war, shall be exercised under the supervision and control of the Secretary of the Treasury," all civil public health activities carried on by any Federal department, sanitary work in connection with ship-yards, supervision of all medical and sanitary matters in industrial plants having contracts with Ordnance Department, codes for protection for health workers in war industries, were placed under the Public Health Service.

The report is a comprehensive volume of 373 pages, embracing eight sections together with recommendations of the Surgeon-General and a financial statement with statistical report.

The Scientific Research Division has been exceedingly active, as shown in the report by investigation of epidemics, causation and control in different parts of the country. The division of Pharmacology has demonstrated a new and perhaps ideal standard for the biological assay of the active principle, derived from the posterior lobe of the pituitary gland. The new standard, potassium chloride, has the great advantage of permanency and chemical uniformity and if adopted by manufacturers would undoubtedly lead to the marketing of pituitary preparations of constant physiological activity and therapeutic value.

An investigation of vaccine virus causing tetanus in a few cases, demonstrated the possibility of ivory points being contaminated with tetanus spores. A recommendation for an order prohibiting the use of points for dispensing vaccine virus was the result. Also a standardized technique for testing vaccine virus for anaërobic contaminations has been worked out.

Rules and standards for the manufacture and sale of "Arsphenamine," heretofore known under the trade names of "Salvarsan," "606," "Arsenobenzol" and "Arsaminol," were prescribed by the service and promulgated by the Federal Trade Commission. This work alone is to be highly commended, as it permits the American product being used extensively and replacing the former foreign products.

Domestic Interstate Quarantine embraces the second part and deals especially with various water supplies used in interstate commerce, and results of vaccination against small-pox, typhoid and para-typhoid fever. The creation, on July 9, in the Public Health Service, of a Division of Venereal Diseases for controlling these dis-

eases, is discussed at some length. Noteworthy to pharmacists is the recommendation of "Prohibition of drug store prescribing for venereal diseases."

Extra-cantonment sanitation for the protection of the military forces is discussed quite extensively in about sixty pages, embracing the proper supervision over water, foods, milk supply, proper disposal of human excreta, elimination of breeding places of flies and mosquitoes, together with efficient control of communicable diseases.

Maritime quarantine of such great import for the prevention of the introduction of the various quarantinable diseases occupies considerable data. The grand total of passengers and crew inspected was 1,129,262, and of vessels fumigated, 3,954. For the destruction of rats and mosquitoes on vessels at the mainland stations, 1,108 ships were fumigated with cyanide gas and 1,101 vessels with sulphur dioxide.

Under Sanitary Reports and Statistics, the usual current publications are mentioned together with their wide range of information and their distribution. It is noteworthy that since the ending of the fiscal year, June 30, 1918, up to and including November 9, approximately 129,000 deaths from influenza and pneumonia (all forms) had been reported to the service.

The Personnel states that the close of the fiscal year presented forty-nine pharmacists on duty as follows: First-class, 31; second-class, 15, and third-class, 3. The miscellaneous division mentions the many publications, reprints, distribution and general matters of information distributed through the public-health bulletins.

Concluding with Needs of the Service, the Surgeon-General states that hospital accommodations should be supplied for the treatment of discharged soldiers and seamen. Up to the ending of the fiscal year, there had already been 14,000 patients discharged from the army for tuberculosis alone, and no provision had been made by the army for their care.

Additional funds are asked for to provide for the printing of the highly important and valuable publications of the department.

An appendix embracing the financial statement and a summary of physical examination together with a list of operations performed, ends the report.

This report is very comprehensive, embracing as it does a very wide field of investigation, dealing with every problem of public health and cannot but impress us with the activities of the Public

Health Service in the efforts to guard not only the health of our Army and Navy during the fiscal year, but the entire population of the country. The Public Health Service deserves great commendation for its invaluable guidance in the control of the health of the country.

MITCHELL BERNSTEIN, M.D.

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#### DECEASE OF MRS. E. G. EBERLE.

As we are preparing for publication, the information is received of the demise of Mrs. Eugene G. Eberle, wife of Prof. E. G. Eberle, former president of the American Pharmaceutical Association and now the editor of the *Journal of the American Pharmaceutical Association*, on Sunday afternoon, February 8. Mrs. Eberle frequently accompanied the professor in his attendance at pharmaceutical association meetings. She enjoyed the friendship of the ladies of the pharmaceutical circles and universally endeared herself to them by her kindness and loving and happy disposition. In the death of his dear wife our friend has lost his companion for life and his closest adviser and helpmate. Words fail to express the deep sense of our sorrow and sympathy. Many are the friends who highly esteemed her worth and who will mourn with him as they appreciate his great loss and theirs of a kind and good friend.



# THE AMERICAN JOURNAL OF PHARMACY

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MARCH, 1919

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## EDITORIAL.

### THE POSITION OF THE COMMITTEE ON EDUCATION AND SPECIAL TRAINING IN REGARD TO S. A. T. C. UNITS IN SCHOOLS OF PHARMACY.

Under the above title there is printed in the "Correspondence" in the February number of the *Journal of the American Pharmaceutical Association* the following letter.

#### WAR DEPARTMENT.

Committee on Education and Special Training, Section of Training  
and Instruction Branch War Plans Division, General Staff.

January 18, 1919.

CHARLES H. LAWALL, *President*,  
American Pharmaceutical Association,  
39 South 10th Street, Philadelphia, Pa.

*Dear Sir:* You have requested, as President of the American Pharmaceutical Association, a statement of the position of the Committee on Education and Special Training in regard to S. A. T. C. units in schools of pharmacy. The basis of this request is that the subject has been under discussion by many who are interested in education in pharmacy and in the pharmaceutical journals, and that it is not clear that the position taken by the War Department has been fully understood. With the permission of the Chairman of the Committee on Education and Special Training the following statement is made:

The object of the Students' Army Training Corps was to furnish a supply of educated men from whom officers for the new army could be chosen, and to direct their training while in educational

institutions so that those selected for commissions would more quickly be prepared to assume their duties as officers. It was strictly a war measure, and not an attempt by the government to standardize education. Any effect this plan may have had on the problems of education in any line in peace times is entirely incidental, and this matter received consideration only to the extent that it was the aim of the committee to disturb existing methods of education as little as was consistent with the attainment of its aims.

In the case of pharmacy the fundamental consideration was that the needs of the Army for pharmacists would be satisfactorily met through the draft. Although there was no real necessity for the inclusion of pharmacy students in S. A. T. C. for the purpose of supplying pharmacists for the Army, the Committee, nevertheless, decided that a limited number might wisely be accepted on the basis that this training would also prepare them for service as chemists and in other useful capacities. The plan finally evolved was to recognize those pharmacy schools in institutions which already had S. A. T. C. units, and to limit the admission to those students in these schools who were eligible for the collegiate section. This required graduation from an approved four-year high school, or an equivalent education.

A committee of representative educators in pharmacy, chiefly from the schools which would be eligible under this plan, was consulted September 29, 1918. This committee was requested to draw up a sample course in pharmacy. As in the case of all programs for courses adopted by the committee, this program in pharmacy was not prescribed but was issued as an example of what would be acceptable.

Yours very truly,

Committee on Education and Special Training,

(Signed) By H. D. ARNOLD,

*Lieut.-Colonel, Medical Corps, U. S. A.*

HDA/MNN

The appearance of this *official* statement of the position of the War Department concerning the Students' Army Training Corps units in pharmacy schools and the purpose that actuated the Department in the establishment of these, is welcomed as a conclusive justification of the editorial "A Quasi Recognition of Pharmacy"

published in the November, 1918, issue of the AMERICAN JOURNAL of PHARMACY.

The previously announced position of the then Surgeon-General Gorgas "that the needs of the Army for pharmacists would be satisfactorily met through the draft," is repeated in this official statement and was reflected in the actions of the Committee on Education and Special Training. The decision of the committee to include in the S. A. T. C. the "limited number of students in those pharmacy schools in institutions which already had S. A. T. C. units" and "on the basis that this training would also prepare them for service as chemists and in other useful capacities," indicates that the acceptance of such pharmacy students was incidental and that the real object was "service as chemists and in other useful capacities." In no way can this be construed as a direct and distinct recognition of pharmacy and the language of this official statement bears out fully our characterization of "quasi."

The statements made in certain articles that have appeared in the pharmaceutical journals such as these: "pharmacy had thus been recognized by the government as a profession," "this is a very satisfactory recognition of professional pharmacy," "here, at least, pharmacy came into its own and received the same recognition as was accorded to the other professions," and "the War Department recognized the need of establishing a pharmacy unit in the S. A. T. C. in order to train men for army and civil life," are unfortunately for pharmacy not verified by the facts. The statement made in person to the writer by an official in the Department was that if pharmacists were, really, the need the first consideration would have been given to schools that were not included in the S. A. T. C.

Furthermore, this *official* statement refutes the claim that "the federal government has set a standard for pharmacy." In dulcet tones this theme has been harped upon and spread widecast by those whose desires it would appear had obtunded alike their view of the true situation and their sense of propriety. The object of the S. A. T. C. was to furnish the many thousands of officers that would be needed for the army contemplated, and this should have been well known to all. The body blow to these sentimental strains is now administered by the positive assertion in this letter that: "It was strictly a war measure, and not an attempt by the government to standardize education. Any effect this plan may have had on the



problems of education in any line in peace times is entirely incidental, and this matter received consideration only to the extent that it was the aim of the committee to disturb existing methods of education as little as was consistent with the attainment of its aims."

It is not the intention to continue the polemics displayed in the editorial correspondence in the January issue of the JOURNAL, but this letter of the War Department substantiates our editorial contention so well that its publication was deemed necessary along with a minimum of comment which could also have been greatly amplified. Doubtless the readers who are interested in this question will appreciate the quod erat demonstrandum.

G. M. B.

### PHARMACOPŒIAL REVISION.

The attention of the readers of the AMERICAN JOURNAL OF PHARMACY is directed to a circular letter issued by the Chairman of the Committee of Revision of the Pharmacopœia of the United States published on page 185, requesting that suggestions for corrections, improvements, additions, etc., should be sent to him. The intent is to compile all of these recommendations for presentation to the convention to be called for the Tenth Decennial Revision for the benefit and use of the committee to be then selected for that revision of our national authority for standards.

This is a very timely communication and this appeal for coöperation should be very generally responded to. It is very creditable to the efforts and a testimony to the effectiveness of the service rendered by the Committee of Revision that prepared the Ninth Revision, that so few errors in the text have been found and so few of the standards have been seriously criticized. It has likewise withstood the test of the unusual conditions prevailing throughout the last four years and the period of the world war. Very few indeed have been the changes or corrections required to be made, and it has not been necessary for the committee to issue the Supplement that they were given authority to publish. However, all works of human hands and the minds of men are more or less imperfect and the new knowledge and the new medicines coming into use and others becoming obsolete from disuse are ample reasons that have justified the wisdom of the American method for a decennial revision of our pharmacopœia.

(The AMERICAN JOURNAL OF PHARMACY has always been a prime mover in aiding in the various revisions of the U. S. P. and its pages have contained many papers that have been of very material assistance to the committees that have been charged with the responsibility of preparing the various revisions. No better medium for the presentation of subjects for pharmacopœial consideration is offered and its columns continue to be open for such matters and especially welcome are papers containing recommendations for amendment or improvement in the official formulas or standards.

It is opportune to call attention at this time to the fact that the next United States Pharmacopœial Convention is scheduled to meet in the city of Washington in May, 1920. As many of the medical, pharmaceutical and chemical organizations, who are properly represented in this convention, will hold their meetings for 1920 after the date named, these organizations should not fail to select their accredited delegates at their various meetings held during the present year. The importance of membership and representation in this convention should not be overlooked.

G. M. B.

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## THE STUDY OF DRUGS.

BY DR. FRED. B. KILMER.

The advice of the most successful men in our calling is to "stick to drugs." Keep drugs and medicinal appliances to the forefront. Let your customers know that you keep a drug store. Put in side lines when you find that they will pay, but use them to increase your regular trade.

The people of the United States, in congress assembled, have defined the word "drugs" to mean all medicines and preparations recognized by the United States Pharmacopœia, or the National Formulary, for internal or external use, and all substances or mixture of substances intended to be used for the cure, mitigation or prevention of disease, either of man or animal.

This literally means that every substance that can in any way whatever be used in medicine or in surgery, belongs to the drug store. The range is large enough to tax the capacity of the ordinary pharmacy. It is for the drug trade to get, and to hold fast to, that which belongs to it.

To the man who bewails that there is no future in pharmacy, to the young man looking for an opening, I commend a study of the foregoing definition of drugs, as a possible chance to secure a foothold for himself and to "cash in" on his diploma. In other words, I commend to him a study of drugs.

Materia medica and therapeutics today present a broader and a wider field than ever before in their history. Drugs need more than ever the careful study of the trained mind of the pharmacist. Pharmacy is not the selling of cigars, soda water, confectionery, stationery and knick-knacks, although it is true that these may by force, form a part of the modern stock, and must be dealt in to keep the business going. Pharmacy is not the simple selling of drugs, or handling them over the counter in prepared packages. Real pharmacy is the integral part of the great science of medicine and surgery, and has to do with all the allied applications of the healing art. Yea, it even extends out to, and has to do with, hygiene, and the wonderful coming forme of preventive medicine.

The pharmacist should know, from its beginning, every substance in any way connected with the application of these sciences. He should know them from a to z, in their every aspect. How else can he be a pharmacist, or become a master of his calling?

He should know drugs, and all there is to be known about them. Ordinarily the pharmacist learns, either in his apprenticeship or the college, the names of the most commonly used drugs, and the preparations made therefrom. Perhaps he memorizes the doses of potent drugs. The rest of his knowledge is gained from the label, or a quick reference to the Dispensatory, or to the manufacturer's catalogue.

Few pharmacists, especially the younger men, have a thorough knowledge of even a quarter of a hundred drugs. How many can speak, upon their own authority, as to the pharmacology and the therapy of any appreciable percentage of the drugs which they handle every day?

Here then is an opening in pharmacy—the study of drugs. That the pharmacist should know the pharmacology of drugs, will probably not be questioned. But the objection may be made that emphasis laid upon the therapeutic action of drugs by the pharmacist has a tendency to counter-prescribing. The reverse is probably true. Counter-prescribing is now most largely carried on empirically, by



men who have only a superficial knowledge of drugs, and with whom it is often a matter of chance and extensive guessing.

The pharmacist who has a real knowledge of pharmacology, and the therapeutic action of drugs, would probably be the last to prescribe. To know even the physical characteristics of a drug, its active principles, its constitutional formula, its dose, without knowing its uses, its functions, its effects upon the system in health and in disease, is like knowing the names of the organs of the body without knowing their functions.

Who shall know drugs except the pharmacist? The physician's knowledge of *materia medica* in a large number of instances is not profound. During his college course, at the present day, he can give *materia medica* and therapeutics but scant attention. The limited hospital pharmacopœia and the manufacturer's literature often make up his library. He has no time or opportunity to really study drugs.

A knowledge of drugs would enable the pharmacist to extend the physician's *materia medica*, to assist him in choosing the right form, to realize his intentions, and it might help him to overcome the medical man's habit of office dispensing of a limited number of drugs. Even a conversational knowledge, covering the range of conventional and recognized drugs, would help to fill the physician's prescription with really useful preparations.

A knowledge of drugs makes a pharmacist a pharmacist, places him in his right position—a master of his profession—a position that the medical profession and the public are bound to recognize, and from which he cannot be dislodged.

Here is a list of drugs, the most of them in quite common use: aconitum, aloes, ammoniacum, arnica, belladonna, cannabis, indica, capsicum, cascara, cinchona, conium, digitalis, ergota, gelsemium, hydrastis, hyoscyamus, ipecacuanha, jalapa, krameria, lobelia, nuxvomica, opium, podophyllum, rheum, senega, serpentaria, stramonium, sumbul, valeriana, yerba santa.

Let us ask ourselves a few questions about them. It will be especially good practice for the student.

Without consulting a text-book, could you describe their characteristics as to appearance, taste and odor?

If they were laid out on a table, unlabeled, could you recognize and name them?

What are their chief therapeutic properties?

These are simple, almost foolish questions. Any junior in college ought to be able to answer them. Young men "cram" up on these very drugs in order to pass the board of pharmacy.

Now, let us see all that we know, all that everybody else knows, and maybe we will come to the conclusion that there is much yet to be found out about these everyday drugs; that there is in many of these commonplace substances opportunity for long and earnest study, opportunity for the pharmacist to make a name for himself, to do a great work for the science of pharmacy and medicine, and bestow untold benefits upon his fellow-man.

Let us take up one or two of them in alphabetical order:

*Aconite*.—The books say it contains the powerful principle, aconitine. Its chief characteristic properties are defined as "anodyne, diaphoretic, sedative; a powerful sensory nerve stimulant." Page after page in the books tells of its origin, history, structure, chemical composition, pharmacology, physiological action, uses, doses, etc. Knowledge beginning in the far distant past, accumulated, recorded and handed down to us. Incidentally, we find there are a number, but not quite "57," varieties of aconite and while the books don't say which is which, the species known as *aconitum napellus* is official, and for the most part the value of the other sorts is not recorded. Possibly some of the other kinds are "just as good," maybe they are better—who knows.

A test laid down for the so-called powerful principle is to take a piece of aconite root, chew a bit of it, and there results a peculiar tingling or numbing, quite appreciable on the tongue and roof of the mouth.

Aconite grows in the temperate zones of the northern hemisphere, including the United States. (It is cultivated in gardens.)

Find the growing plant and chew a piece of the fresh root. You will notice first a sweet taste, and the odor of radish. Upon chewing for a time, aided by the action of saliva, the tingling and numbness appears. On drying the root, the odor, color and taste change.

The so-called active principle is evidently not in evidence in the growing plant. Question: Is this powerful principle developed in drying the plant? If so, would the method of handling and drying influence the character and the amount?

The pharmacopœia, and other books, set forth certain preparations of aconite, and tell us how to prepare them. Powders, pills, tinctures, fluid extracts, solid extracts, liniments, etc.

Which of these preparations most truly represent the anodyne, diaphoretic and sedative properties of the drug?

Experience has shown that some of them are unreliable, in that they are highly active under some conditions, as under other conditions, some of them are practically inert. Which of these preparations would you advise a physician to choose as best exhibiting any one of the three characteristic properties? Which is the best for anodyne effects? Which for diaphoretic effects? Which for sedative effects? Which of these preparations represent the whole drug? Which will give the results the prescriber seeks for?

Let us pass on to *aloes*, a drug known and used in medicine centuries before the Christian era. The books teem with words about it. We learn that solidified juices of the leaves of various aloe are the sources of the several varieties of aloes. We read that its most potent principle is a rather variable substance called "aloin." That from aloes the chemists have separated a number of remarkable substances—resinous, crystalline, amorphous, extractive and the like.

The characteristic actions of aloes, we learn, are defined as "cathartic, hepatic, stimulant." That in small doses it acts as a stomachic, in large portions as an emmenagogue.

How much do we, as pharmacists, know of the difference in action between the several varieties of aloes? What have we determined as to whether the crude methods by which the juice is gathered and prepared, have any influence upon its action? Which of our preparations best exhibits the action of aloes as a cathartic or hepatic stimulant? Which preparation is best when a stomachic is desired? Which when an emmenagogue is wanted? Which preparation represents aloes in all its phases? Do our preparations take into account the aloin or the many resinous and crystalline derivatives found in aloes?

Now let us consider *belladonna*. This is one of the most ancient drugs known to medicine. Thousands upon thousands of pages, and hundreds of volumes, have been written about it. All through the ages belladonna has grown more prominent, and stands today as one of the most useful drugs in materia medica. Any graduate in pharmacy could write a thesis on belladonna, and would possibly claim (at least at graduation) that he "knows all about it."

What do we know? What does anybody know? What is the sum of our knowledge of belladonna?



The things which a pharmacist ought to know about belladonna are delineated in the Pharmacopœia and the Dispensatories, and I advise every young pharmacist to read carefully what these have to say about belladonna. The history of the drug is a most interesting study from every point of view. It would take too long to attempt to describe here the chemical, pharmaceutical and physiological properties of this drug. It has a stated action. It is an anodyne, anti-spasmodic, stimulant, anti-sudorific and mydriatic. It has effects, peculiarly its own, on the nervous system, the respiratory system, the glandular system and the secretive system, and this action exists when taken internally, as a drug, or applied as a plaster.

As pharmacists we are most interested in its active principle. What is the active principle of belladonna? The usual answer is "atropine." Is this the correct answer? Investigation has shown that atropine does not exist in cultivated belladonna, nor indeed in belladonna when carefully handled and dried. Atropine is a product, or a derivative, produced during the manipulation of the drug. In assaying belladonna in the laboratory atropine is produced during the process, and is taken as the standard for estimating the alkaloidal value of the drug. Here is a table showing the various constituents which have been found in belladonna by various observers.

*Constituents of Belladonna.*—Atropine, hyosyamine, belladonnine, atropamine, apoatropine, starch, malic acid, chrysotropic acid, lexatropic acid, succinic acid, prendatorine, phyteumscolla, atosine, chlorophyl, potassium salts, magnesium salts, calcium salts, sodium salts, ammonium salts, acetic acid, gums, resins, mucilage, asparagin, albumin, etc. This is quite an array. Certainly there is something present in belladonna besides atropine.

There are four or five alkaloidal bodies associated or combined with numerous other constituents, all of which in some measure make up the physiological and therapeutic action of belladonna. It may be stated with confidence that neither a solution of atropine, nor the salts of atropine, seem to possess the full qualities of the extract of belladonna. "Admixtures of extractives with the alkaloid cannot fully replace natural belladonna extractives that are of the same alkaloidal proportions."

Prof. Lloyd has stated: "In my opinion the term 'derivative' will apply better to belladonna ultimates than constituents." All

alkaloidal bodies, possibly, are only derivatives, and atropine is only an artificial derivative which, by common consent, is used as a measure of the drug.

Many problems surrounding belladonna await investigation by the pharmacist. Do the tincture, solid extract, ointment and the like, represent belladonna in its entirety, or are they only solutions of atropine, or some of the other derivatives? Is alcohol the best solvent for the actual constituents of belladonna? If so, what strength alcohol is likely to give the more eligible preparation in every respect—physiological, therapeutic and pharmaceutical? There is much to be learned before we can say that we have reached the top in respect to our galenical preparation of belladonna.

We are now cultivating belladonna in relatively large quantities in this country (possibly 500 acres in 1918), and in this cultivation we have learned something. We can increase the size of the leaf and the root. We can in a measure control and increase the amount of the so-called active principle. We have found that different results follow the handling of the plant from the seedlings to the mature and ripened plant. There is a difference in the physical appearance, size, taste and odor of the plant itself when we vary the mode of collecting and curing. Cured at one stage of growth, when the crop matured, cured at another stage, or gathered at another stage of growth, and allowed to sweat and become subject to enzymic action, gives an entirely different product from that obtained from other modes. Just how important these different methods of preparation may be, or what method is best has not yet been fully determined.

We seem to see that the alcoholic extract of the green leaf is quite different physically from that prepared from the root.

The problems connected with the cultivation of belladonna have been at times baffling. It was not an easy task to acclimatize belladonna from the moist cool climate of Europe, to the dry, hot atmosphere which abounds in our land. It was difficult to inure it to our soil, but we have succeeded in producing thrifty plants with an increased yield of alkaloid principles. American grown belladonna, in most respects, is far superior to the wild product from its native soil. Now comes the task of the study of the pharmacological properties of American grown belladonna.

There is not time to go through the list of drugs given in our schedule; each of these presents a theme for study and research.

Some of them have, since the beginning of the war, been among the list of scarce drugs, and we have been sorely tried with supplies of doubtful origin and usefulness. At times we have been compelled to look for substitutes. We may with profit ask—Which of our preparations best exhibit the physiological and therapeutic properties of the drug? If a drug has more than one action, what preparation represents these separate actions? In making a pharmaceutical preparation of these drugs do we take into account all of the constituents of the drug?

The solvent now most commonly used for vegetable drugs is alcohol. Alcohol is becoming a very expensive solvent and difficult to procure. It may be that there is a better solvent for many drugs. Workers have become convinced that a substance other than alcohol should be found for use as a solvent for many vegetable principles. Possibly we are following precedence rather than actual knowledge in the percentage of alcohol which we use for the extraction of drugs. Here are a few of the problems which will occur to every worker in drugs: Alcohol of 95 per cent. is a solvent for a certain range of constituents. Alcohol 50 per cent. strength gives us an entirely different range of substances. Which percentage is best adapted to each?

If we moisten a pound of the drug with our menstruum, and pack in a tall, narrow percolator and proceed to percolate in the conventional manner, by pouring on the drug a pint of alcohol, we will see that when it proceeds through the drug it becomes loaded with extractive, and its solvent power changes. Its solvent power at the last inch is quite different from its solvent power at the first inch. The second pint of menstruum will be brought in contact with the drug and constituents left behind, or perhaps only partly carried over with the first pint which passed through. With every step every new addition of menstruum, and every new percolate you will have a different action. When we have finally reached the point where we can say we have extracted all of the principles, we find that the menstruum will still dissolve something.

If we take our percolate from the drug made, say with 80 per cent. alcohol, and put the liquid in an evaporating dish and set the dish over a flame and evaporate the menstruum, the result will be a sticky mass which we call the solid extract. This, we say, represents the drug. Now, if instead of evaporating the liquid over the fire we pour it into thin films and allow warm air to drive off



the menstruum, we will again have produced a solid mass which it will be found presents quite a different appearance from the other extraction. In short in subjecting the vegetable drug extractive to prolonged heat we change its character—we cook it, and the delicate vegetable principles all become changed during the process of evaporation and concentration. Lloyd says that in these drugs the so-called alkaloids are in a colloidal form. Undoubtedly prolonged heating will produce a change in vegetable colloids, but as related to medicinal substances no one has fully investigated these changes.

To the younger men of the profession, let me suggest, there is much yet to be developed in the chemistry and the pharmacy of our best known drugs. Let us be pharmacists and devote our most earnest attention to the study of drugs.

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## BALLOTA HIRSUTA, A RECENT ADULTERANT FOR MARRUBIUM VULGARE.

BY HEBER W. YOUNGKEN, PH.D.

The writer recently secured a sample of a shipment labeled "horehound herb" that had been sent from a Greek port to a Philadelphia firm, but which was condemned by the government on the ground that it contained an adulterant. A cursory macroscopic examination failed to reveal the presence of any foreign leaf or stem, but critical observations showed it to contain a number of suspicious looking calyxes, much broader and more velvety in appearance than those common to *Marrubium vulgare*. He immediately set out to identify the foreign calyx, which presented characteristics of some *Ballota* species, and, after a lengthy search, came upon a single specimen in the herbarium of The Academy of Natural Sciences of Philadelphia, that was found identical with the calyx in question and which was labeled "*Ballota hirsuta* Benth." Upon looking up the characteristics of this species in Benthani's "Labiatum Genera et Species," p. 595, he found the macroscopic aspects of the calyx identical. Through the courtesy of Professor Stewardson Brown, of the academy, he procured a leaf and calyx from a herbarium sheet, and these were studied comparatively with the foreign calyxes and fragments of leaves found in the sample. These agreed in every detail. Later the herbarium sheet of *Ballota hir-*

*suta* was borrowed and further macroscopic and microscopic details apprehended which proved conclusively that the adulterant was *Ballota hirsuta*. The characteristics of these two herbs and the important diagnostic differences are hereby presented.



FIG. 1.

FIG. 2.

FIG. 1. Aërial portion (to right) and branch (to left) of *Marrubium vulgare* L.  $\times \frac{1}{3}$ .

FIG. 2. Aërial foliage and floral stem of *Ballota hirsuta* Benth. Note the dense axillary clusters of flowers.  $\times \frac{1}{3}$ .

*Marrubium vulgare* Linnæus.

*Marrubium vulgare* L. (Fig. 1) commonly known as horehound, hoarhound, white hoarhound, or marvel, is a perennial herb indigenous to Europe and Central Asia. It is cultivated in various parts of the United States and has escaped in waste places throughout North America. The underground portion consists of a short rhizome bearing numerous slender rootlets. The aërial stem is erect, quadrangular, .3 to .8 M. high, 3 to 5 mm. in diameter,

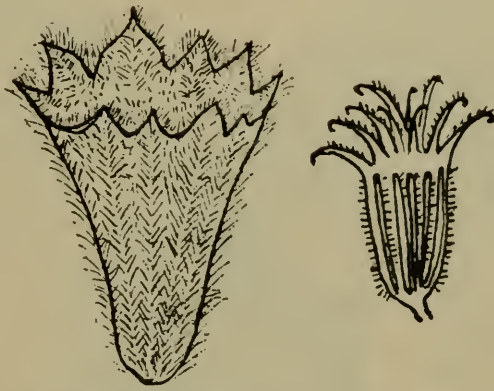


FIG. 3. Calyx of *Marrubium vulgare* to right; calyx of *Ballota hirsuta* to left.  $\times 4$ .

branched, the branches ascending. Its white-wooly aspect is very striking. The leaves are opposite, petiolate, exstipulate, varying from ovate to broadly ovate to nearly orbicular in outline, 1.5 to 6 Cm. in length, 9 to 25 Mm. in breadth; apex obtuse; base narrowed or rounded or sub-cordate; margin coarsely crenate; upper surface downy-whitish, lower surface woolly; venation pinnate-reticulate. The inflorescence is a verticillaster with flowers arranged in dense axillary whorls, each having a tubular sparsely pubescent calyx 6-7 Mm. long, with 10 subulate, recurved, bristle-like teeth (Fig. 3, *M*), a whitish bilabiate corolla, four parallel stamens ascending under the upper lid of the corolla, and a bi-carpellary pistil with a four-celled ovary. The fruit consists of four nutlets.

MICROSCOPIC CHARACTERISTICS OF *Marrubium vulgare* L.

The leaf shows the typical dorsoventral lamina common to the genus *Marrubium*. Transverse (Fig. 4) and surface sections show an upper epidermis, devoid of stomata, composed of tabular cells with somewhat undulate outer walls, a layer of vertically elongated



palisade cells, several layers of spongy parenchyma cells traversed by collateral bundles, and a lower epidermis similar to that of the upper, but possessing stomata. Non-glandular and glandular trichomes are present as outgrowths on both upper and lower epidermis. They are, however, more numerous on the lower epidermis. The non-glandular trichomes are either simple or branched,

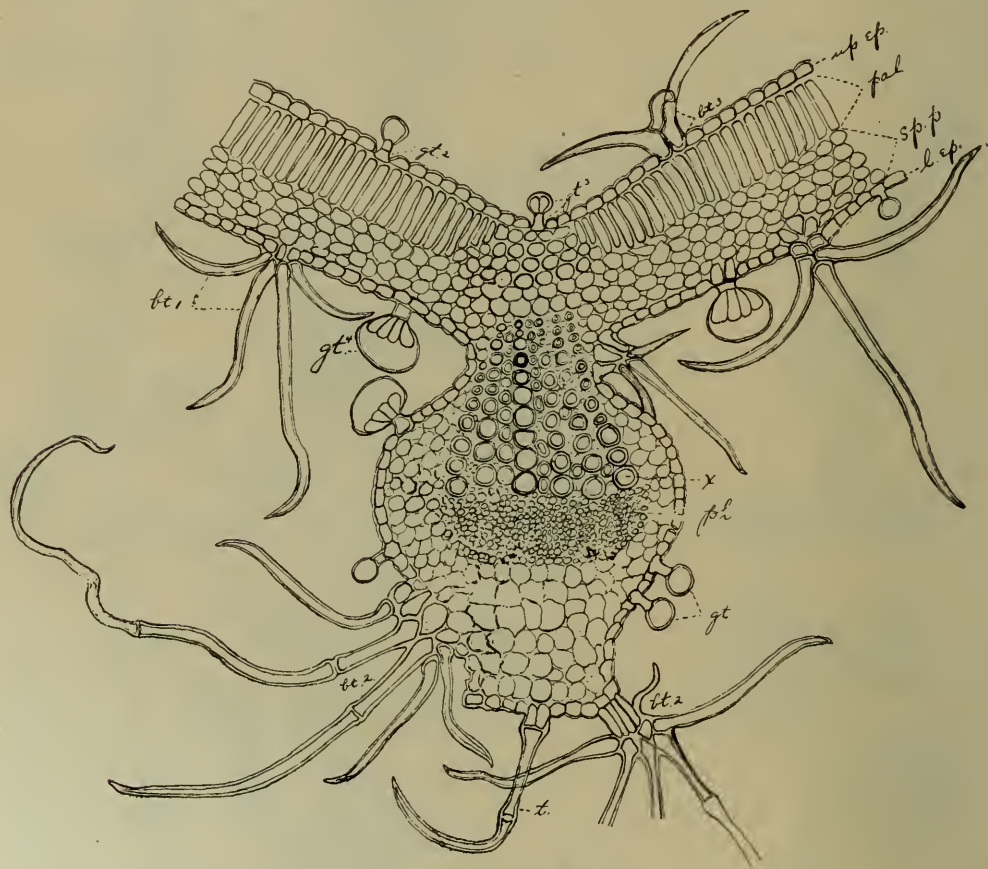


FIG. 4. Cross section through one of the stronger veins and portion of the lamina of *Marrubium vulgare*. *up. ep.*, upper epidermis; *l. ep.*, lower epidermis; *pal*, palisade parenchyma; *sp. p.*, spongy parenchyma; *x*, xylem; *ph.*, phloem; *t*, long-pointed non-glandular trichome; *bt<sup>1</sup>*, *bt<sup>2</sup>*, branched trichomes, more or less stalked; *bt<sup>3</sup>*, sessile branched trichome; *gt*, *gt<sup>2</sup>*, *gt<sup>3</sup>*, *gt<sup>4</sup>*, several types of glandular trichomes.  $\times 120$ .

the latter type predominating. The simple trichomes are, for the most part, unicellular and almost invariably slightly curved. There occur, however, a scattering of much elongated, characteristically curved and twisted (in dried material) unicellular hairs which type predominate on the stem, giving this part its white-woolly aspect (Fig. 5, *J*). In addition to these, uniseriate two-celled hairs with the distal cell long-pointed and bent have been met with occasionally.

The branched trichomes are of two kinds, viz.: (1) those that project directly out of slightly elongated epidermal cells and which are two to three branched and (2) those which consist of a more or less elongated central multicellular stalk with radiating branches (Fig. 4). As many as fifteen branches have been observed on this type. Of these, those emanating from the base of the stalk are unicellular, and more frequently curved than straight, while those

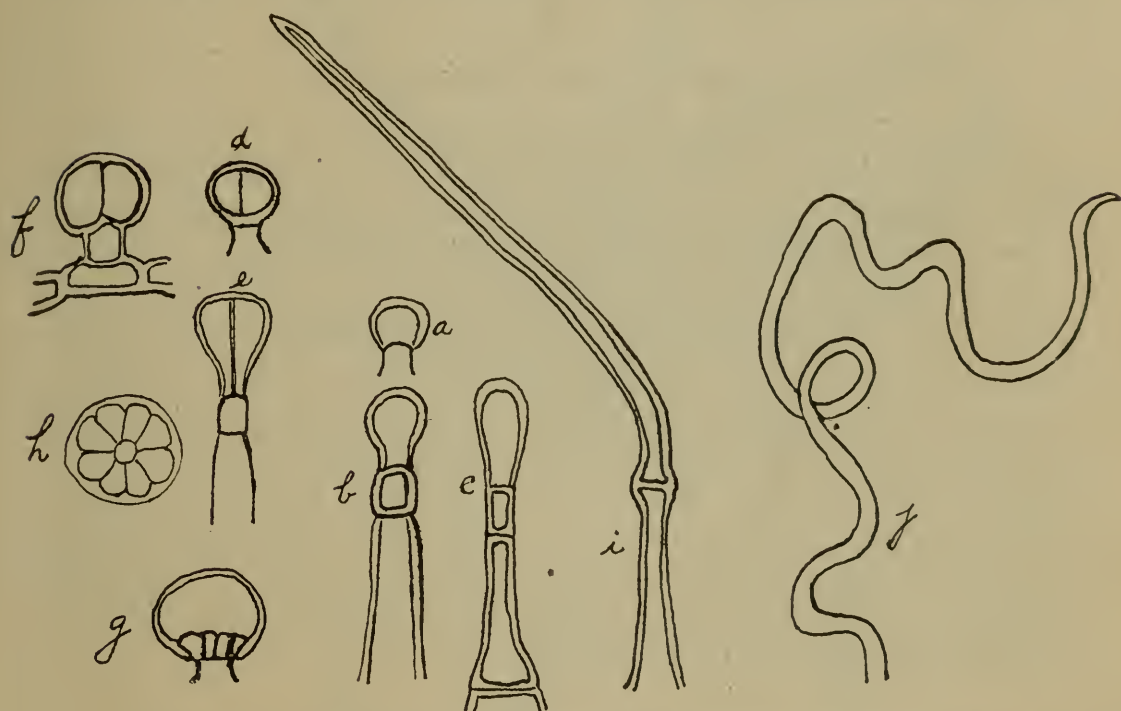


FIG. 5. Various types of hairs found on *Marrubium vulgare*. *a, b, c, d, e, f, g, h*, glandular hairs, and *i*, non-glandular two-celled hair, all found on the foliage leaves and calyxes; *j*, curled unicellular-non-glandular hair, a type abundantly found on the stem that gives to this part its white-woolly appearance. *a, d, f*, glandular hairs with a one-celled stalk and a one- to two-celled head; *b, c, e*, glandular hairs with two-celled uniseriate stalk and 1-2-celled head, the distal cell of the stalk being considerably shortened and forming the "neck cell"; *g*, side view, and *h*, view from above of large balloon-shaped glandular hair with one-celled stalk and 8-celled head. (All highly magnified.)

issuing from points higher up are either unicellular or two- or three-celled, the distal cell of these last being characteristically long, pointed and curved. The central stalk of the branched trichome does not usually attain the great length of the similar part of the branched trichome of *Ballota hirsuta*.

The glandular trichomes have either a one- to two-celled short or long stalk and a one-, two- or eight-celled balloon-shaped glandular head. The large number of the last mentioned (balloon) type which possess unicellular short stalks is very striking (Figs. 4 and 5).

Sections made through the calyx show to a modified degree the peculiar microscopic structure of the foliage leaf. The lamina is thinner and more trichomes of the glandular variety are evident.

*Ballota hirsuta* Benth.

*Ballota hirsuta* Benth. is a perennial hirsute herb, which is indigenous to Mediterranean countries. The herbarium specimen examined (Fig. 2) presented the following macroscopic peculiarities: Stem quadrangular, pubescent but not white-woolly like *Marrubium*. Leaves, opposite, petiolate, ovate to orbicular, coarsely hairy on upper surface, coarsely whitish-woolly on under surface, apex obtuse, base sub-cordate, margin crenate, venation pinnate-reticulate. Inflorescence a verticillaster, the hermaphrodite flowers appearing in dense axillary clusters and usually fewer in number than in the verticillasters of *Marrubium*. Each flower consists of a bilabiate infundibuliform calyx, up to 10 Mm. long (Fig. 3, B) with limb showing a margin of 10 broadly acute or mucronate teeth, a distinctly bilabiate corolla, four included stamens, and a bi-carpellary pistil. The fruit consists of four nutlets.

MICROSCOPICAL CHARACTERISTICS OF *Ballota hirsuta* Benth.

Transverse sections (Fig. 7) made through the lamina region of the foliage leaf show typical dorsoventral structure. Passing from ventral to dorsal surface the following structures present themselves for examination:

Upper epidermis, devoid of stomata and composed of tabular cells with outer walls more or less convex and showing a rather thick cuticle. Directly beneath this tissue is a layer of somewhat loosely arranged vertically elongated palisade cells, the average being shorter than those found in *Marrubium vulgare*. Beneath the palisade layer are several layers of more or less loosely arranged spongy parenchyma cells, irregular in shape. Through this region course numerous collateral fibro-vascular bundles marking the positions of the veins. The tracheæ of these have strongly lignified



walls, The most prominent peculiarities are shown by the trichomes which thickly cover both surfaces. These appear nearly equal in number as outgrowths of the epidermises. Both non-glandular and glandular types are represented. As for *Marrubium vulgare*, so for this leaf, the non-glandular trichomes fall into three categories,

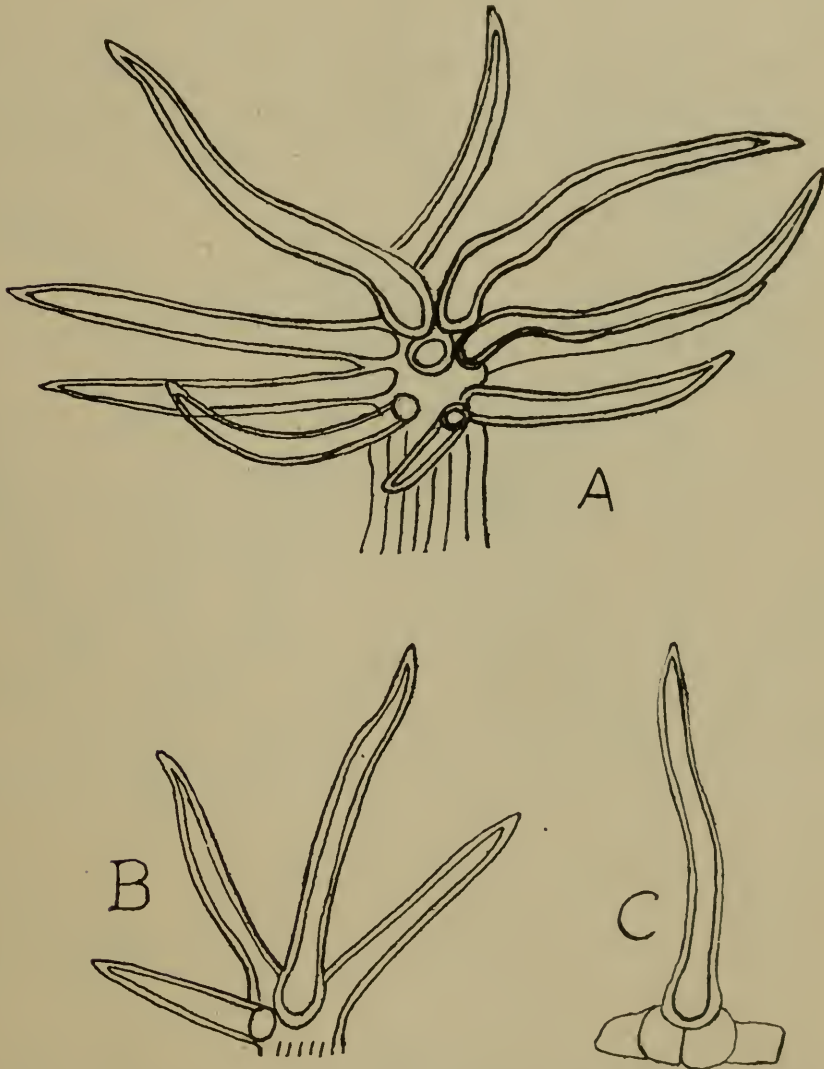


FIG. 6. Non-glandular hairs from calyx of *Marrubium vulgare*. *A*, many branched hair with somewhat elongated stalk; *B*, branched hair with short stalk and few branches; *C*, non-glandular unicellular hair. (All highly magnified.)

viz.: unicellular, uniseriate, and branched. The unicellular variety are either short or long, straight or bent over toward the epidermis. The individual cells of the uniseriate hairs form distinct articulations. By far the most conspicuous and diagnostic elements are the

branched hairs (Fig. 8). These are easily distinguished from those of *Marrubium vulgare* by their generally longer basal stalks, thicker walls and more rigid looking branches. As many as eighteen



FIG. 7. Cross section of foliage leaf of *Ballota hirsuta* made through a stronger nerve and portion of the lamina. *up. e.*, upper epidermis; *l. e.*, lower epidermis; *pal.*, palisade parenchyma; *sp. p.*, spongy parenchyma; *s*, stoma; *col.*, collenchyma; *si.*, sieve tissue; *tr.*, trachea; *wf.*, wood fibers; *bt.*, branched trichomes; *glt.*, branched trichome with central branch the longest and bearing a two-celled glandular head; *gt¹*, *gt²*, *gt³*, glandular trichomes.  $\times 98$ .

branches have been counted emanating from the central stalk. The shortest branches arise from the basal portion, the rest becoming longer as the stalk is ascended. Most of the branches vary from one to three cells in length. The central or longest branch, however, may be uniseriate four-celled and attain a length of 3 Mm.

A form of branched trichome has been observed by the writer that stands out preëminently as constituting the most easy and practical histologic means of distinguishing *Ballota hirsuta* from *Marrubium vulgare*. This trichome resembles the other branched forms seen in *Ballota* but differs from these in respect to the central branch which has a two-four celled uniseriate stalk and a glandular head of one or two to four cells (Fig. 8, *A*).

The glandular trichomes exhibit various forms (Fig. 9) viz.: (*a*) short one-celled stalk and small unicellular head; (*b*) short unicellular stalk and large four to eight-celled balloon-shaped head; (*c*)

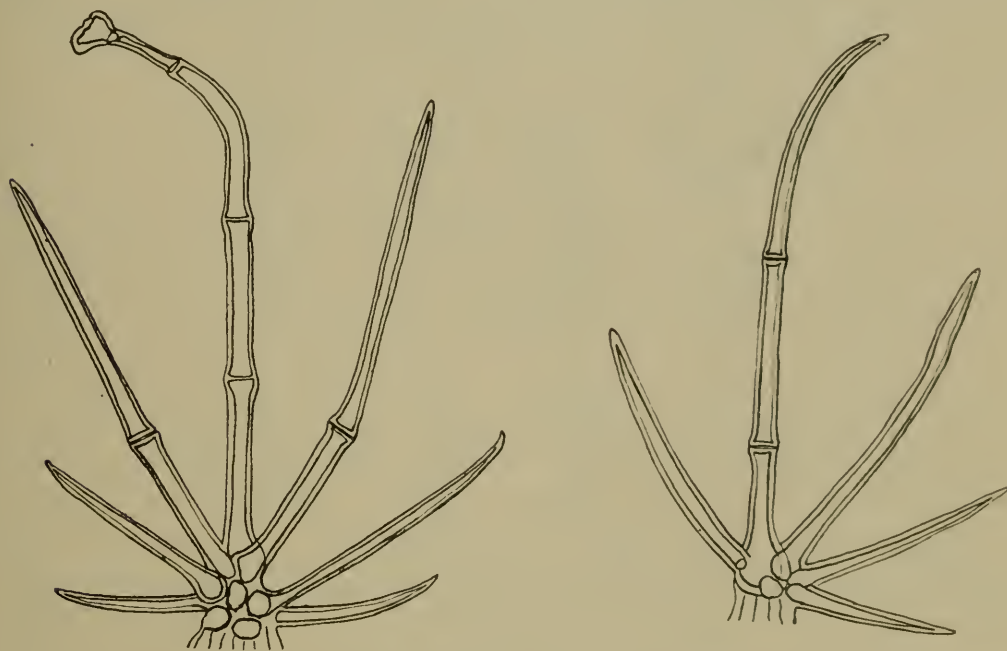


FIG. 8. Types of branched hairs found on the foliage leaves and calyxes of *Ballota hirsuta*. The illustration to the left shows one of these, the central branch of which is longer than the rest and bears a glandular head at its summit. (Highly magnified.)

long one-celled stalk and small spheroidal unicellular head; (*d*) long one-celled stalk and elongated unicellular head; (*e*) one-celled stalk and two-celled head; (*f*) short two-celled stalk and two-celled head; (*g*) long two-celled stalk, the distal cell ("neck cell") being shorter than the proximal one and bearing a one-celled head. Many of the hairs have their basal portions lignified. These take a pinkish to reddish coloration with phloroglucin and concentrated hydrochloric acid.

The calyx of *Ballota hirsuta* shows a microscopic structure simi-



lar to that of the foliage leaf, but on a reduced scale. The tendency for more of the branched hairs to show the central branch glandular has been observed.

The chief practical diagnostic differences between *Ballota hirsuta* and *Marrubium vulgare* are as follows:

1. The calyx, which in *Ballota hirsuta* is densely hairy, distinctly bi-labiate-infundibuliform with limb margin showing 10 broadly acute or mucronate teeth, whereas in *Marrubium vulgare* it is sparsely hairy, distinctly tubular with ten bristle-like recurved teeth.

2. The absence in *Marrubium vulgare* and presence in *Ballota hirsuta* of certain branched trichomes, the central branch of which bears a glandular head or one of two to four cells.

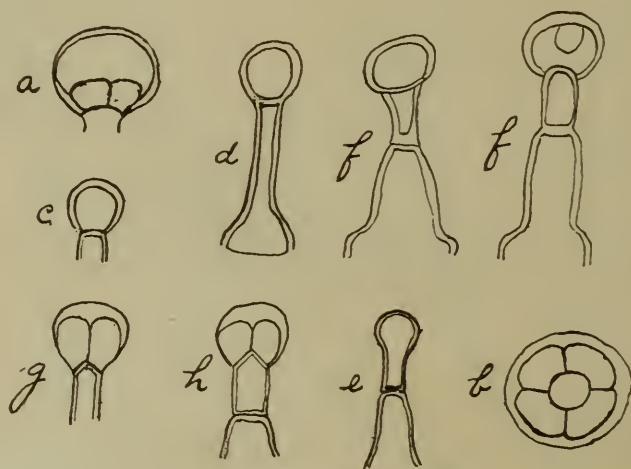


FIG. 9. Various types of glandular trichomes found on the calyx and foliage leaf of *Ballota hirsuta*. *a*, lateral view, and *b*, view from above of the balloon type of glandular trichome showing (in *a*) a short unicellular stalk and (in *b*) a four-celled glandular head; *c*, *d*, *e*, *f*, *g*, other types of glandular hairs having a 1-2-celled stalk and a 1-2-celled glandular head. (All highly magnified.)

3. The branched trichomes of *Ballota hirsuta* show on the average longer basal stalks, thicker walls and more rigid branches than those of *Marrubium vulgare*.

4. A number of trichomes of *Ballota hirsuta* are lignified at their bases, whereas in *Marrubium vulgare* no such lignification has been observed.

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#### LITERATURE.

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## A REVIEW OF THE ADVANCES IN PHARMACY.

BY JOHN K. THUM, PH.M.,

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*The Potash Situation.*—In 1914, the United States Geological Survey and the Bureau of Soils were given funds to undertake an investigation as to the possibility of developing the potash industry in this country. This investigation has proven of considerable value and the results are the beginning of what will eventually prove to develop into a great American industry.

Since 1914 wonderful progress has been made. Only recently Secretary Lane optimistically declared that within two years this country will be independent of outside sources of potash. What this means may be readily imagined from the fact that our pre-war demands and necessities for this important substance amounted to well over 1,000,000 tons, nearly all of which was imported. The question of an adequate potash supply is a vital one, and of far-reaching economic importance.

One of the first sources of this substance to be investigated was the vast deposit of kelp along the Pacific coast from Mexico to Alaska. At first the kelp was merely dried or incinerated and ground to powder. It was afterward found that it could be handled in a more profitable manner which would result in the production of other valuable chemicals, with potash relegated to the position of a by-product. As an example, the Hercules Powder Company at San Diego, California, has built a large plant where the kelp is not dried, but fermented, yielding not only potash, but acetone, iodine and other products, including algin, which it is predicted may ultimately become commercially valuable.

Investigation has revealed another source of potash in the United States and that is the flue of blast furnaces and the dust of cement kilns. The production of potash from this source requires a rather highly technical operation, and is mainly carried out by means of an apparatus known as the Cottrell electrical precipitator, in which the potash is separated out and collected by electrostatic precipitation. Many iron ores, especially those of Alabama, contain about three per cent. of potash, most of which is recoverable. It is esti-

mated that if all the blast furnaces in the United States installed this process, nearly 1,000,000 tons of potash could be obtained from this source alone. From the cement works, where the potash is collected in the same manner, the Bureau of Soils estimated from investigations carried out, that the cement kilns could, in the aggregate, yield nearly 100,000 tons of potash each year.

Another source of potash in this country is the salt lakes, which are particularly interesting and seem to promise great things in the way of making this country independent of other countries for our potash. One of these wonderful lakes—Searles Lake, in California—consists of a vast mass of salt crystals about twelve square miles in area and seventy feet deep, all the water having evaporated. A bulletin issued by the United States Geological Survey, makes the statement that the main central salt deposit is a firm and very porous bed of salt crystals; indeed it is so firm and hard that roads are made on it, and it is no uncommon thing for teams and motor trucks to drive over its surface, and even the concrete foundations of the American Trona Corporation's pump house were laid on the surface. The average potash content is four per cent. in the form of the chloride. This corporation is producing about 4,500 tons of crude potash salts per month, and is also turning out about 50 tons of borax per day.

Other sources of potash which are looked upon as promising are the mineral silicates, such as feldspar, sericite, and alunite. In Marysville, in southern Utah, the Mineral Products Corporation has already put up a plant with an output at present of about 600 tons per month of sulphate of potash. There are signs that aluminum as well as potash will ultimately be obtainable from these minerals; indeed, it is predicted by some investigators that this may prove a better course of aluminum than bauxite. With all these sources of supply for this very necessary substance let us hope that prices will soon drop to reasonable proportions.<sup>1</sup>

*Quinine-Formaldehyde Solution in War Surgery.*—The advantages claimed for this solution are that it is easily prepared, is stable, can be readily concentrated for transportation, the strength can be easily increased or diminished, and it can be used in an early stage of wound treatment, at the field or evacuation hospital. The formula for the solution is as follows:

<sup>1</sup> *The Living Age*, vol. 13, 1919, 183.



Quinine sulphate .....	1.00 gm.
Acid hydrochloric .....	0.50 mls
Acid acetic (99 per cent.) .....	5.00 mls
Sodium chloride .....	17.50 gms.
Liquor formaldehyde, U. S. P. ....	1.00 mil
Thymol .....	0.25 gm.
Alcohol (90 per cent.) .....	15.00 mls
Distilled water .....	q. s. 1,000.00 mls

Dissolve the quinine in the acids; dissolve the sodium chloride in the water; dissolve the thymol in the alcohol; mix the first two solutions and add to this mixture the formaldehyde solution, and then to the combined solutions add the thymol solution.

The technic for the application of this solution is similar to that used in the treatment of wounds by the Carrel-Dakin solution, or it may be injected through the Carrel tubes every two hours, or more frequently, if necessary, to keep the wound bathed with it.

Its efficacy was pretty well tried out in a series of 100 badly infected wounds at the American Red Cross Military Hospital No. 5, many of which were compound comminuted fractures, which had been treated for from ten days to two weeks or longer with Dakin's solution, and in which the bacterial flora showed no signs of decrease in the great majority of cases. There was a marked drop in temperature and pulse in many cases on changing from Dakin's to quinine-formaldehyde solution, without any operative procedure. Some wounds showing a count of 10 to 15 bacteria per field apparently have been rendered free from germs within three days. That is to say, none have been found in the repeated examination of fifteen fields. Thirty consecutive cases treated within thirty-six to forty-eight hours after receipt of injury, on whom preoperative smears were made and the presence of infection established, were rendered sterile within forty-eight hours and have continued to show absence of any bacteria on repeated counts subsequently, with one exception.—*Annals of Surgery*, Philadelphia, vol. 68, 1918, 467.

*Feeding Experiments with Raw and Boiled Carrots.*—Any contribution that will add to our present scanty knowledge of vitamins is surely worth-while recording. Denton and Kohman feel that in the present food crisis a knowledge of the dietetic properties of root vegetables is of prime importance, and especially so since the use of dehydrated vegetables promises to come into general vogue. In their experiments they found that carrots, when properly reinforced

with starch, casein, butter or lard, and salts, to such an extent that 50 per cent. of the caloric value of the diet is still derived from the carrots, will produce normal growth and reproduction in albino rats. Carrots as an exclusive diet, except for the addition of chlorine, calcium, phosphorus, sodium, may support animals in apparently good health for as long as sixteen weeks. The animals on such a diet maintain and very often increase their body weight. It was demonstrated that carrots contain an unusually large amount of both the water-soluble and fat-soluble vitamins. They believe that ordinary methods of cooking do not materially injure the nutritive value of carrots, certainly not when used as part of a mixed diet. They are convinced that a considerable portion of the caloric value of the food is lost when the water used in cooking is rejected.—*Jour. Biological Chemistry*, Baltimore, vol. 36, 1918, 249.

*Determination of Citral*.—According to Parker and Hiltner in making determinations for citral by the latter's colorimetric method with metaphenylenediamine hydrochloride it will happen at times that lemon and orange oils and extracts give blue or green colors in place of yellow, which makes the use of this method more or less restricted. Investigation showed that this was due to oxidation of some constituent of the citrus oil, and experiments tended to show that the addition of a certain amount of oxalic acid to the original Hiltner reagent would be a most practical way of preventing such blue coloration. The reagent as modified by them is made by dissolving 1 gram of the metaphenylenediamine hydrochloride and 1 gram of crystallized oxalic acid, each in 45 mls of 80 per cent. alcohol; the two solutions are then mixed and the volume brought up to 100 mls with 80 per cent. alcohol. This solution is then shaken up with three grams of fuller's earth and filtered. They give detailed information as to the use of this colorimetric method and the necessary calculations.—*J. Ind. and Eng. Chem.*, vol. 10, 1918, 608, through *The Analyst*, Nov., 1918.

*The Output of Platinum*.—In conjunction with the usual uses to which this valuable metal is put, namely electrical appliances, crucibles, etc., the requirements were greatly augmented during the war on account of the increased needs for internal combustion engines for airplanes, automobiles, tanks and motor boats, the manufacture of fuming sulphuric acid, for which the metal is em-

ployed as a catalyzer, the acid being one of the prime needs in the making of munitions, and in the fixing of nitrogen from the air, which in turn is used for manufacture of explosives. Before the war 90 per cent. of the world's output of this métal was produced from Russia. The Russian and the newer and less developed field in Colombia, South America, comprise the world's two important sources of the valuable metal. In spite of the great demand for this metal in carrying out important manufactures engendered by the war, the production in Russia fell from 300,000 ounces in 1911, to about 78,000 ounces in 1916. However, to sort of counteract this decrease in production from this source, production in the Choco district of Columbia increased from 12,000 ounces in 1911 to nearly 50,000 troy ounces in 1917, which is an increase of 300 per cent in this practically new field. It undoubtedly will be a source of satisfaction to American manufacturers who need this metal to know that they have easy access to this promising field instead of depending on far-off chaotic Russia.—*Jour. Amer. Med. Assoc.*, vol., 72, 1919, 411.

*Narcotic Drug Control.*—The new law dealing with this important matter in the state of New York became effective on February 1. Plans for its enforcement have been formulated which authorize representatives to visit all persons or institutions having authority to possess, dispense or prescribe habit-forming drugs to ascertain if their records comply with the law, and in case of violation to bring the offender to account. In a communication to the New York County Medical Society the commission having charge of the enforcement of the law make clear that it realizes that many of the problems are administrative, educational and medical rather than legislative, as was shown by the testimony brought out at the hearings of the legislative investigating committee. Therefore the commission desired to so administer the law as to hamper the honest physician as little as possible. It was also announced that it would be the commission's purpose to so administer the law that those unfortunates, the drug addicts, will be cared for and safeguarded against the growing evil. This commission evidences a desire for the coöperation and assistance of all the medical organizations of the state in controlling and eventually eradicating this pernicious evil and doing away with abuses practised by some of those legally entitled to possess and dispense drugs of this kind.—*Jour. A. M. A.*, vol. 72, 1919, 431.



*Idiosyncrasies to Drugs.*—Civalleri comments on the fact that the term medicinal anaphylaxis is coming to be used instead of the old term idiosyncrasy. He discusses the literature on the subject, especially that in which quinine is involved. Among other instances, he makes note of a case mentioned by Pereira in which a second injection of quinine, given fifteen years after the first injection, gave rise to a train of grave symptoms that could only be explained as anaphylactoid phenomena in a previously sensitized individual. Civalleri confirmed this experience of Pereira's by experiments of his own on guinea-pigs. Serious and sometimes fatal phenomena were induced almost constantly by parenteral injections of quinine in previously sensitized animals in doses which normal guinea-pigs tolerated perfectly. Effects were most pronounced with intervals of from three to twenty days. The smallest sensitizing dose, by the peritoneum, was 0.04 gram. As quinine cannot be said to be an antigen, and as there is no production of antibodies with it, the reaction cannot be called a true anaphylaxis, although it is closely analogous. Civalleri would describe it as an allergy to a non-antigenic substance; he says that it may be acquired or congenital or inherited. —*Rivista Critica di Clinica Medica*, Florence, vol. 19, 1918, 421.

*Preliminary Report of Method for Estimating in Vivo Germicidal Activity of Antiseptics.*—With the idea of reducing the margin of error in estimating the bacterial contents of a wound with microbe charts Perkins and his associates have been culturing the wounds, counting the number of colonies and plotting curves as in microbe charts. To reduce the element of personal equation the work has been done by one man. Inoculations were made from the same part of the surface of the wound, one definite spot being selected and used throughout; the same platinum wire loop was used each time in an endeavor to get a uniform sized drop. The drop obtained was inoculated at the bed-side in 2 mls of plain bouillon, the bouillon suspension, undiluted, was immediately poured over an agar-agar plate, which was then covered and turned upside down and marked with the patient's number, the number of the culture, and the time the culture was taken. The plate was then taken to the laboratory and placed in an incubator and kept at 37° C. At the end of twenty-four hours the colonies were counted, macroscopically, and recorded. Carrying out this procedure during different stages of wound treatment with antiseptics some idea can be

obtained of the comparative strength of antiseptics and the length of time during which they are active when applied to human tissues in the presence of infection.—*Annals of Surgery*, Philadelphia, vol. 3. 1918, 68.

*Carbon Tetrachloride Vapor as a Delousing Agent.*—Dr. Foster, of the United States Public Health Service, gives out a preliminary report on experiments for the destruction of lice in clothing by the vapor of carbon tetrachloride. Heat and hydrocyanic gas are undoubtedly the best agents for this purpose, but require a rather complicated apparatus for their use and can be used to advantage only where the work is to be done on a large scale. The experiments were undertaken to find some agent that could be used anywhere and for small operations. Carbon tetrachloride vapor was found to be effective after two hours exposure with the clothing rather closely packed in a tin or other vessel that is air-tight, in an amount of 25 mils. The clothing to be disinfected should not occupy more than half or two thirds of the containing vessel. In these experiments only the lice were killed. The nits were only partly killed, but their hatching was delayed. The method evolved was simple; the material was packed in the can, on top of which was placed several layers of filter paper, on which was poured the carbon tetrachloride. The can was then covered with several thicknesses of toweling and a loose cover placed over this. In some experiments, the lice-infested material was wrapped tightly in papers; various combinations of carbon tetrachloride with gasoline were also tried out. It was found, however, that unadulterated carbon tetrachloride was more effective and the lice were always killed in about the time mentioned. At the present price of carbon tetrachloride, the cost for treatment of the clothing of a single soldier will amount to from one and a half to five cents.—Public Health Reports, October 25, 1918.

## EXAMINATION OF A SAMPLE OF GUM ASAFÆTIDA.

BY EDO CLAASSEN,  
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A piece of gum asafœtida, in which whitish, shining specks could be seen, was subjected to an examination to determine its purity. It weighed 9.310 Gm. By extracting it with hot water, followed by some alcohol, it left a residue, composed of particles of rock, partly whitish and shining, partly grayish with black spots. The first proved to be calcite and the others granite, the black spots in this being amphibole; their weight was 4.241 Gm. The granite particles, one of which weighed 0.820 Gm., could be easily separated by a pair of pincers; they weighed 0.935 Gm., so that the calcite amounted to 3.306 Gm. It will be seen that the adulterations represented nearly half the quantity of the gum, the percentage being gum 54.45 per cent., calcite 35.51 per cent. and granite 10.04 per cent.

The adulteration of another piece of gum, previously examined, consisted of calcite only in about the same amount.

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A NOTE ON CRYSTALLIZED GALL STONES.

BY EDO CLAASSEN,  
EAST CLEVELAND, OHIO.

Quite a number of interesting bodies were passed by a woman, 45 years old. Most of them were small, grainlike; several, however, were of a larger size, up to that of a pea. Their color was yellowish, somewhat shining. Heated on platinum foil, they melted at first, then evaporated, leaving a little of a dark substance and when ignited, burned with a yellow flame. They dissolved in hot alcohol, the solution leaving, when evaporated on a slide, four-sided rhombic plates; the largest crystals, being polyhedral with a diameter from 6 to 10 millimeters and weighing up to 0.384 Gm. One of these, particularly, weighing 0.208 Gm., surpassed the others by its quite regular shape; it belonged to the regular (the tesseral) crystal system, being a combination of the predominant cube with the octahedron and the dodecahedron =  $00\ 0\ 00\cdot 0\cdot 00\ 0\cdot$ , which was proven by measuring its angles by means of a hand goniometer. All the above properties are known to be such, as belong to cholesterin, which in fact they represent.



## IS IT WORTH WHILE?<sup>1</sup>

" I was having a long talk to one of my colleagues last night, and we were discussing how doubtful we felt as to whether it was worth while continuing to take an active interest in pharmaceutical affairs. The opinion we came to was that it was a matter of individual temperament. My own opinion is that there can be no half measures. 'Taking an interest' means giving up time, energy, recreation, and even cash. Unless a man is prepared to work on these lines, he had better resign and be done with it.

"Yours, feeling rather stale,

"X. Y. Z."

The above letter reached us a few days ago from one of the leaders of Australian pharmacy. It typifies in a general way the feeling that every man who takes an interest in public affairs experiences at some time or other during his career. Despondency as to practical results achieved by his efforts, annoyance at the indifference and lack of appreciation of the rank and file, and irritation because of the conservatism of some, and the disloyalty of others are factors which invariably lead to the heart-searching question: "Is it worth while?"

The ethics of voluntary service presupposes a willingness to make personal sacrifices. There are compensations, it is true, but these cannot always be tangibly expressed. The hope of reward is not always present to sweeten the labor. Each man knows his own duty best. To some the call to public service is insistent. Every individual more or less possesses some of the characteristics which make for good citizenship. In pharmacy in particular the craft has never lacked men of foresight and character as its leaders. Today quite as much as in the past the need for leadership of the right sort exists. The best minds of all engaged in the craft should be available, and in no sense are they too good to be utilized for the advancement of the cause which every true pharmacist has at heart. But it should not be overlooked that in addition to those excellent qualities already mentioned, patience, persistence, and perseverance are equally important. Time is always on the side of the reformer. Often the steady plodder accomplishes more in the long run than his more brilliant and scholarly colleague. Few reforms

<sup>1</sup> Reprinted from *The Australian Jour. of Phar.*, November 18.

are gained without long periods of preparation. Pharmaceutical history amply illustrates this. How much pharmacists to-day owe to the early pioneers for years of faithful service is hard to say. Their deeds live after them, and we know that their memory is both cherished and honored.

Edmund Burke in "Thoughts on the Cause of Present Discontents" says that "The man who lives wholly detached from others must be either an angel or a devil. . . . We are born only to be men. We shall do enough if we form ourselves to be good ones. It is therefore our business carefully to cultivate in our minds every sort of generous and honest feeling that belongs to our nature. To model our principles to our duty and our situation . . . and rather to run the risk of falling into faults in a course which leads us to act with effect and energy, than to loiter out our days without blame, without use. Public life is a situation of power and energy; he trespasses against his duty who sleeps upon his watch as well as he that goes over to the enemy."

Burke's eloquence might well act as a guide and stimulus to those who are inclined to falter in their work. The call to service is insistent in the hearts of men. Whether little or much results from their efforts depends to a great extent upon the amount of enthusiasm and energy they give out themselves and inspire in others. No one can truthfully say that service of this kind faithfully rendered is not worth while. It would be a thousand pities if because of some temporary discouragement there should be any diminution in the ranks of those to whom pharmaceutical service means not merely a perfunctory duty or drudgery, but an exemplification of good citizenship in the performance of which all that is best in them finds truthful expression.

## A NEW METHOD FOR THE DETERMINATION OF VANILLIN IN VANILLA EXTRACT.<sup>1</sup>

BY ARTHUR W. DOX AND G. P. PLAISANCE,

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The official method for the determination of vanillin in vanilla extract consists essentially in removing the alcohol, extracting the vanillin with ether, crystallizing it from the ethereal solution and weighing it directly, identifying the crystals if necessary by their melting point. This method was first proposed by Hess and Prescott.<sup>2</sup>

Modifications were subsequently introduced by Winton and Silverman,<sup>3</sup> and by Winton and Bailey.<sup>4</sup>

For details of manipulation reference should be made to the official methods of the A. O. A. C.<sup>5</sup>

The whole operation is rather lengthy and tedious.

Methods dependent upon the precipitation of vanillin by various reagents have been suggested but have not come into common use. Hanus<sup>6</sup> used m-nitrobenzoylhydrazide as a precipitant, and also platinic chloride<sup>7</sup> for estimating vanillin in the presence of piperonal. Moulin<sup>8</sup> converted the vanillin into a yellow methyl picrate and estimated it colorimetrically. More recently Folin and Denis<sup>9</sup> have devised a colorimetric method based upon the color obtained by means of phosphotungstic and phosphomolybdic acids.

The writers<sup>10</sup> have found that thiobarbituric acid in the presence of 12 per cent. hydrochloric acid is a general reagent for the precipitation of aromatic aldehydes and have applied it to the quantitative determination of furfural<sup>11</sup>. Under these conditions vanillin gave with thiobarbituric acid an insoluble vermilion colored pre-

<sup>1</sup> Reprinted from *Simmons' Spice Mill*, November, 1918.

<sup>2</sup> *J. Am. Chem. Soc.*, 21, 256 and 719, 1899.

<sup>3</sup> *Ibid.*, 24, 1128, 1902.

<sup>4</sup> *Ibid.*, 27, 719, 1905.

<sup>5</sup> *Bur. Chem. Bull.* No. 152, p. 146.

<sup>6</sup> *Zeitschr. Untes. Nahr. Genussm.*, 10, 585, 1905.

<sup>7</sup> *Ibid.*, 10, 657, 1900.

<sup>8</sup> *Bull. Soc. Chem.*, 29, 278, 1903.

<sup>9</sup> *J. Ind. Eng. Chem.*, 4, 670, 1912.

<sup>10</sup> Dox and Plaisance, *J. Am. Chem. Soc.*, 38, 2164, 1916.

<sup>11</sup> Dox and Plaisance, *ibid.*, 38, 2156, 1916.



cipitate, which analysis showed to contain the percentages of nitrogen and sulphur required for the simple condensation product, 3-methoxy-4-hydroxybenzalmalonylthiourea. Since the reaction appeared to be practically quantitative, we decided to test out its possible application as a means of quantitatively estimating vanillin.

The first experiments were conducted with a standard solution of pure vanillin. Aliquots of this solution were precipitated with thiobarbituric acid in the presence of 12 per cent. hydrochloric acid. The total volume of the reaction mixture was 50 Cc. The precipitates were allowed to stand over night, then filtered on Gooch crucibles, washed with 50 Cc. 12 per cent. hydrochloric acid in small portions and finally with 20 Cc. of water. The results are set forth in the following table:

Van. Taken, G.	Weight of Precip, G.	Van. Recov.	Error, Mg.
.0200	.0330	.0180	-2.0
.0200	.0337	.0184	-1.6
.0200	.0336	.0184	-1.6
.0200	.0330	.0180	-2.0
.0500	.0877	.0480	-2.0
.0500	.0890	.0487	-1.3
.0500	.0885	.0484	-1.6
.0500	.0890	.0487	-1.3
.0500	.0888	.0486	-1.4
.0500	.0906	.0496	-0.5
.0500	.0900	.0492	-0.8
.0500*	.0890	.0487	-1.3
.0500*	.0890	.0487	-1.3

In each case the filtrate was a lemon-yellow color, indicating that a small amount of the condensation product remained in solution. This observation is further substantiated by the fact that the vanillin recovered is somewhat less than the amount taken. The error is, however, quite uniform, regardless of the amount of vanillin taken, averaging 2.6 Mg. of the condensation product or 1.4 Mg. vanillin. It is apparent therefore that a solubility correction must be applied just as in the determination of furfural by the official phloroglucinol method.

Before applying the method to the determination of vanillin in commercial vanillin extracts, where clarification is necessary, the use of lead acetate as a clarifying agent was tested. In the last two determinations in the above table, lead acetate was added and the

\* Clarified with lead acetate.

excess removed from the filtrate by hydrochloric acid before adding thiobarbituric acid. The results are in close agreement with the other results, showing that the small amount of lead chloride remaining in solution does not interfere with the determination.

A sample of vanilla extract of known purity was next used. The procedure was as follows:—25 Cc. of the extract were dealcoholized in the usual manner, then transferred to a 50 Cc. standard sugar flask and filled to the mark with lead acetate solution. After standing for several hours at about 37° C. the contents of the flask were filtered through a dry filter. The filtrate was a straw color, indicating the absence of caramel as added coloring matter. 40 Cc. of this filtrate was then transferred to another 50 Cc. flask. Sufficient concentrated hydrochloric acid was added to bring the volume to 50 Cc. and the acidity to 12 per cent. After standing a few minutes the lead chloride was removed by filtration through a dry filter and 40 Cc. of the filtrate taken for the determination. On adding thiobarbituric acid in 12 per cent. hydrochloric acid solution, an orange-colored precipitate resulted, indistinguishable in color from the product with pure vanillin. However, the color of the filtrate was somewhat darker than with vanillin alone, due no doubt to the original color of the filtrate after clarification. The precipitate was allowed to stand over night filtered on a Gooch crucible, washed with hydrochloric acid and water as in the previous determination and dried at 98°. The results were as follows:

Vanilla Extract Taken, Cc.	Aliquot Per Cent. of Extract Taken.	Wt. of Precipitate, G.	Wt. of Precipitate Corrected for Solubility.	Vanillin found in Aliquot.	Vanillin in 25 Cc. Extract, G.	Vanillin in Extract Per Cent.
25	64	.0450	.0476	.0260	.0406	0.16
25	64	.0450	.0476	.0260	.0406	0.16
25	72	.0501	.0527	.0288	.0400	0.16
25	72	.0498	.0523	.0286	.0397	0.16
25	72	.0510	.0536	.0293	.0407	0.16
25	72	.0501	.0527	.0288	.0400	0.16
25	72	.0502	.0528	.0289	.0401	0.16
25+	80	.0890	.0916	.0501	.0626	0.25
25+	80	.0882	.0908	.0496	.0621	0.25

The above method is not applicable to artificial extracts where caramel is added as a coloring matter, since caramel contains furfural derivatives which react with thiobarbituric acid. The absence of caramel should first be demonstrated qualitatively. When caramel is present, the filtrate after clarification is brown instead of

straw-colored. A still more delicate test, described here for the first time, is the reaction with phloroglucinol. After clarifying and removing the excess of lead as chloride, phloroglucinol is added. In the presence of caramel a brown precipitate is formed. If caramel is absent, the vanillin gives a delicate rose-pink color or a slight pink precipitate. Clarification of the sample is necessary, as shown by the fact that the two determinations without clarification gave high results.

#### SUMMARY.

Thiobarbituric acid, which is easily prepared from malonic ester and thiourea, may be used for the quantitative determination of vanillin in vanilla extracts which do not contain caramel as added coloring matter. When caramel is present it may easily be detected by the brown precipitate formed on the addition of phloroglucinol to the clarified extract containing 12 per cent. hydrochloric acid.

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### CHLORAMINE REACTIONS OF PROTEINS.<sup>1</sup>

BY J. F. BRIGGS.

The attention which has been paid to the use of hypochlorous acid in antiseptic surgery in recent times has indicated the necessity for a clear exposition of the chemical functions of the chloramines generally and of the chloramine derivatives of the proteins in particular. A complete discussion of the clinical aspect of the subject recently appeared in a paper read before this society by Dr. T. Rettie,<sup>2</sup> and reference may also be made to publications by Dakin and others.<sup>3</sup> The object of the present note is to recall attention to the important researches of Raschig,<sup>4</sup> in which the reactions of the chloramine group were outlined, and a process for the preparation of hydrazine by means of these reactions was established. About the same time, Cross, Bevan and Briggs<sup>5</sup> found in Raschig's results the explanation of certain hitherto obscure facts in connection with flax bleaching, and indicated the future importance of this general

<sup>1</sup> Reprinted from *Journal of Society of Chemical Industry*, December, 1918.

<sup>2</sup> *Ibid.*, 1918, 23 T.

<sup>3</sup> *Ibid.*, 1915, 919, 977; 1916, 651.

<sup>4</sup> *Ber.*, 1907, 40, 4586; *Chem.-Zeit.*, 1907, 31, 926.

<sup>5</sup> *Ibid.*, 1908, 261.



reactivity of the amino group. As an industrial operation the chlorination of wool had long been known, and the physical modification produced by the treatment utilized, but the persistence of the active chlorine in the treated protein was considered more or less as a technical perversity rather than a fundamental consequence of the reaction.

Our investigation of this wide subject did not pretend to be exhaustive, and many "loose ends" were left both in the qualitative and quantitative aspects of the subject. Raschig's original work related only to the monochloramine group,  $\text{NH}_2\text{Cl}$ , or in the case of organic amino compounds  $\text{RNHCl}$ , and the circumstances under which the second hydrogen atom is replaceable by halogen were left undecided. This uncertainty, coupled with the susceptibility of the products to progressive decomposition, led to the failure which we subsequently encountered in our attempts to establish an easy iodometric method for the estimation of amino nitrogen in solution, after removing the excess of hypochlorite by hydrogen peroxide and the excess of the latter by shaking with black manganese dioxide. Positive results were obtained for a large variety of compounds, but their variation with the time and temperature factors caused us to abandon hope of producing a workable analytical process.

All kinds of protein derivatives give the chloramine reaction regardless of their state of complexity and solubility. Thus, complex protein colloids like silk and wool combine with the halogen without entering into solution, gelatin in aqueous solution is precipitated in the form of an insoluble chloramine, peptones, albumoses and simple amino derivatives give chloramine compounds which are soluble in their respective degrees. This wide range through all grades of colloids and colloidal solutions to crystalloids explains the observation that at certain stages colloidal chloramines may be absorbed from old bleaching liquors by vegetable fibers. Certain observations made in those early days are worth recalling in view of the physiological interests which this group of compounds has attained. It was suggested at that time that the persistent odor which clings to the hands after immersion in hypochlorite solutions was due to protein chloramine, and this suggestion appears to have been fully corroborated. Other cases of "chemical" odors developed in bleached fabrics have been traced to a similar cause.

In the recent clinical publications great stress has been laid on the alkalinity of hypochlorite solutions and on the necessity of

counteracting this alkalinity by the addition of a weak acid. It must, however, be pointed out that part of this reputed alkalinity of the hypochlorite solution may really be the result of the chloramine reaction. It is certainly the case that a solution of sodium hypochlorite adjusted to complete neutrality by titration still feels strongly "caustic" to the hands. This is explained by reference to the original reaction  $\text{RNH}_2 + \text{NaOCl} = \text{RNHCl} + \text{NaOH}$ . Whenever a chloramine is formed from a neutral hypochlorite, caustic alkali is liberated, and it would be interesting to ascertain whether this equation is capable of affording a volumetric analytical method. Alkali acts to a certain extent as a stabilizing agent on the chloramines, and, on the other hand, when a neutral chloramine decomposes, hydrochloric acid is liberated according to the reaction  $3\text{RNHCl} = \text{N}_2 + \text{RNH}_2 + 3\text{HCl}$ . From these two equations the advantage in surgical work of the addition of a polybasic acid, such as boric acid, capable of giving amphoteric salts, becomes very obvious.

In our technical investigations we paid special attention to the chloramine reactions of gelatin as typical of the group, depositing it on cotton yarn as an aqueous solution, and fixing it in the form of insoluble chloramine. This treated yarn, after thorough washing, still retained the active chlorine reaction. Previous combination with formaldehyde did not affect the normal course of the reaction. If a cake of dry gelatin is steeped in a hypochlorite solution for several hours the outside is converted into a hard layer of insoluble chloramine, but the gelatin swells in the ordinary manner. If it be then washed and transferred to hot water, the gelatin of the interior dissolves and is liberated by puncturing the outer skin, leaving an empty bag of gelatin chloramine. It is possible that this phenomenon might be utilized in diffusion experiments, and the chloramine membrane might exhibit special semipermeable effects. When the gelatin chloramine is dried in the oven it is decomposed with the evolution of gas and development of free hydrochloric acid.

As a qualitative test for localized deposits of proteins the chloramine reaction is unexcelled. Stains of protein fluids on fabrics, the presence of wool fibers in cotton, the presence of glue or casein in adhesives and coatings, are easily demonstrated by chlorinating, washing, and developing the color reaction with potassium iodide and starch. The most minute fragment of the sample will suffice for the test, and in special cases the original sample of fabric may

be restored uninjured by treating with an "antichlor" after performing the test. The localization of protein in plant tissues can be demonstrated in the same way by the treatment of their sections; for instance, a thin slice of potato shows a very beautiful network.

Enough has been said to indicate the wide field of research which is open for the development of the quantitative relations of this interesting reaction in the light of recent discoveries, and particularly for the study of the functions of the peculiar form of "active chlorine" which characterizes the group, and which reacts with iodides in the proportional equivalent of  $\text{Cl}=\text{I}_2$ . What are the limits of its oxidizing activity? For example, it readily oxidizes iodides, arsenites and sulphites, but apparently will not bleach coloring matters. If it is conceded that the antiseptic value of hypochlorites is due to the formation of protein chloramines, what is the chemical explanation of the antiseptic action of the chloramines themselves either as formed in the tissues or as applied in the form of pharmaceutical preparations? The essential characteristic of the group is instability, and its relationship to the highly explosive nitrogen chloride would account for this. C. F. Cross patented the preparation of methylene chloramine from formaldehyde-ammonia,<sup>6</sup> which is also somewhat explosive, but it is recognized that certain classes of chloramines, including those of the nitrogenous colloids, are, comparatively speaking, stable compounds.

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## NOTE ON TRYPSIN, AND A NEW METHOD OF PURIFYING ENZYMES.<sup>1</sup>

By JOSEPH T. WOOD, F.I.C.

In a paper entitled "A new method of isolating trypsin," L. Holzb<sup>2</sup> refers to some work carried out by Robertson,<sup>3</sup> who found that when one drop of a saturated solution of safranin is added to 5 or 10 Cc. of neutral, or very faintly alkaline, 0.5 per cent. solution of Gr<sup>3</sup>bler's trypsin, a light, flocculent, colored precipitate slowly appears and gradually settles. It was assumed that the substance pre-

<sup>6</sup> Eng. Pat. 15,303 of 1909; *ibid.*, 1910, 976.

<sup>1</sup> Reprinted from *Journal of Society of Chemical Industry*, December, 1918.

<sup>2</sup> *J. Biol. Chem.*, 1913, 14, 335.

<sup>3</sup> *J. Biol. Chem.*, 1907, 2, 317.



precipitated by safranine is actually trypsin, since the supernatant liquid, although containing substances precipitated by alcohol, is practically free from enzymes. Holzberg has repeated Robertson's experiment. To solutions of Grüber's trypsin, Fairchild's trypsin, and aqueous extracts of sheep's pancreas, he added three eighths of the volume of a 0.8 per cent. solution of safranine. The precipitates were collected and washed, and their proteolytic action tested by digesting with a solution containing 2 Gms. of casein (Gross test). The results are given in the following summary: The substance which is precipitated by the addition of safranine to aqueous solutions of Grüber's or Fairchild's trypsin, or to aqueous extracts of pancreas, has a strong proteolytic action, contains safranine, is very sparingly soluble in water, and insoluble in organic solvents. After the substance has been removed from aqueous solutions of commercial trypsin or pancreas extract, a considerable quantity of a substance remains in solution, which is precipitable by alcohol, and in the case of pancreas extract, a further precipitate is obtained by means of an alcohol-ether mixture (three to one). These substances are practically devoid of proteolytic activity.

I repeated this experiment by adding a 0.1 per cent. and also a saturated solution of safranine to various infusions containing trypsin. An aqueous extract of the pancreas gave a considerable precipitate, which behaved in exactly the same way as the precipitate obtained by Holzberg. Instead of using the Gross test, I used the gelatin test.<sup>4</sup> I found it impossible to separate the precipitate from the filter, as it dried into a horny film. The paper was therefore cut up into small pieces, and in order to obtain some quantitative data it was cut into one-inch squares, which were weighed, and these were then ruled into 100 divisions and the small squares placed in the gelatin tubes. It was found that six squares liquefied, but five did not. The approximate weight of precipitate on one square inch, assuming it to be uniform, was 5.5 mgrms. The precipitate on 0.01 sq. in. would therefore be 0.055 mgrms., so that the quantity of dry precipitate which is active lies between 0.33 and 0.27 mgrm.

Since the whole of the gelatin was liquefied, it was evident that the substance causing the liquefaction was soluble, and it therefore seems that Holzberg, by washing his precipitate, has removed considerable quantities of enzyme. On repeating the experiments with one of my own trypsin preparations, which was comparatively free

<sup>4</sup> *Journal of Society of Chemical Industry*, 1912, 1105.

from albuminous matter, I was surprised to find that no precipitate was formed, *i. e.*, the ordinary preparations of trypsin, and aqueous extracts of pancreas, gave precipitates, but the purified preparation (the strength of which was equal to that of the crude preparation) gave no precipitate. It appears, therefore, that the matter precipitated by safranine is an albuminous compound, which carries the enzyme down with it, and that the precipitation by this method does not produce an enzyme-safranine compound. The method appears to be analogous to that used by Cohnheim<sup>5</sup> for the precipitation of diastase from saliva by means of calcium phosphate, in which a certain quantity of phosphoric acid was added to saliva and the liquid neutralized with lime water, which caused a copious precipitate of calcium phosphate. This precipitate carried down with it a large proportion of the proteins of the saliva, together with the diastase or ptyalin. The precipitate was then collected by filtration, and extracted with a volume of water equal to that of the saliva originally used. The diastase is slightly more soluble than the proteins, and accordingly passes into solution first. Cohnheim repeated this process several times, and finally precipitated the last extract by the addition of alcohol. This precipitate was collected, washed with alcohol, and dried over sulphuric acid, appearing then as an amorphous white powder, freely soluble in water. The author considered it to be free from proteins as its solution did not yield the usual reactions characteristic of these bodies.<sup>6</sup>

I have not yet had the opportunity to compare the nitrogen content of the purified trypsin with that of the trypsin before purification by the method I am about to describe. This would have an important bearing on the constitution of the enzyme.

On referring to Robertson's book on the proteins,<sup>7</sup> I find that, speaking of his own work two years earlier, he says, in the course of a discussion on the compounds of proteins with dyes, "I have found that in faintly alkaline solution trypsin or some constituent of Grüber's trypsin (nach Spalteholz) forms an insoluble compound with safranine"; from this it appears that Robertson himself was

<sup>5</sup> *Virchow's Archiv*, 1863, 28, 241. J. Reynolds Green, *The Soluble Ferments* (Camb. Univ. Press, 1899), p. 45.

<sup>6</sup> Since writing this paper the author has attempted to apply Cohnheim's method to trypsin, but has been unsuccessful.

<sup>7</sup> *The Proteins* (Univ. of California Publications in Physiology), October, 1909.

doubtful whether the precipitate was a compound of trypsin and safranine.

The method of purification of the enzyme which I adopted is a very simple one, and so far as I know has not been previously described; it depends on the fact that cellulose absorbs the impure compound of proteins and enzymes, and that after drying, the colloidal protein portion adheres firmly to the paper, whereas the enzyme is very easily soluble. The method is as follows:

Ordinary circles of Swedish filter paper (J. H. Munktell) 12½ cm. diam., area 122 sq. cm., ash 0.00095 Gm., averaging in weight 0.87 Gm. air-dry, were soaked in the impure enzyme solution, and dried quickly in a current of hot air. The average increase in weight was 0.054 Gm., *i. e.*, they contain about 6.0 per cent. of added matter, or 0.41 mgrm. per sq. cm. When such paper is placed in water, the enzyme dissolves quickly to a perfectly clear solution in a few minutes, but the colloidal matter with which it is associated adheres firmly to the paper; the solution is filtered after 15–20 minutes, by which time the whole of the enzyme matter is dissolved. If left for a longer time, proteins begin to dissolve, and the enzyme strength decreases.

When a solution of safranine is added to the enzyme solution prepared in this way, no precipitate is produced, and the solution passing through the filter is as active as the original solution, due account being taken of the dilution. The following experimental results were obtained: 1.8366 Gm. of the paper impregnated with enzymes was stirred in 183 Cc. of distilled water for 15 minutes, and then filtered; 0.6 Cc. of the filtrate was found to liquefy the standard gelatin tube under the same conditions as in the test previously described<sup>8</sup> corresponding to 6 mgrms. of the paper. The 6 mgrms. of paper contained 0.34 mgrm. of original extract.

A test of the original extract showed 0.35 mgrm. of matter capable of liquefying the gelatin, but the soluble matter is the 6 mgrms. of paper was found by evaporation of the filtrates to be 0.23 mgrm., so that the enzyme has been purified to this extent; *i. e.*, 35 per cent. of non-enzyme matter has been removed. For comparison it may be useful to give results for Grübler's pancreatin, which I have always used as a standard of comparison: it is labelled "Pankreatin Dr. G. Grübler & Co., Leipzig"; 0.1 Gm. dissolved in about 30 Cc. of alkaline water digests 8–10 Gms. of moist blood

<sup>8</sup> *Journal of Society of Chemical Industry*, 912, 1105.



fibrin; 0.52 mgrm. of the original solution liquefied, and 0.56 mgrm. filtered through paper liquefied, *i. e.*, my purified preparation is  $2\frac{1}{4}$  times as strong as Grüber's trypsin. It may be noted that about 20 per cent. of the Grüber trypsin was insoluble in water.

I do not suppose for a moment that the preparation I have made is a pure enzyme, and I have not been able to ascertain how far the purification can be carried by the above method, but I have reason to believe that the purer the enzyme the less colloidal is its character, and that it will pass through a membrane. Professor Kipping has kindly examined a solution of the purified enzymes with the polariscope in order to ascertain if it is optically active. The solution contained 0.1184 Gm. of solids per 100 Cc., which was a strong solution from the point of view of enzyme activity, being about three times as strong as those I have usually employed. No rotation of the plane of polarization could be detected in a 200 Mm. tube. The following are the minimum quantities of material required to liquefy the gelatin in the test described:—Grüber's pancreatin (unfiltered), 0.56 mgrm.; do. (filtered), 0.52; safranine precipitate from pancreas extract, 0.30; pancreas extract on paper, 0.34; purified enzyme, 0.23 mgrm.

From the above facts I draw the conclusion that the enzyme itself is extremely soluble, whereas the protein matter with which it is associated is difficultly soluble, and this difference in solubility may be used to purify the enzyme.

## DIGITALIS LEAVES: EFFECT ON ACTIVITY OF TEMPERATURE IN DRYING.<sup>1</sup>

BY HERBERT C. HAMILTON.

Since the first attempt<sup>2</sup> to standardize digitalis leaves and the extracts, it has been observed that they vary greatly in activity.

Bennefield,<sup>3</sup> in 1881, using a method almost identical with that suggested in the 9th Rev. U. S. P. for standardizing the digitalis series of heart tonics found a variation of about 500 per cent. in the

<sup>1</sup> Reprinted from *The Journal of the American Chemical Society*, January, 1919. Contribution from the Research Laboratory of Parke, Davis & Co.

<sup>2</sup> *Ber.*, 40, 4586, 1907.

<sup>3</sup> Bennefield, "Ueber Digitalis Tincturen," Inaug. Diss., Göttingen, 1881.

activity of tinctures from digitalis leaves from various parts of Germany.

Bührer,<sup>4</sup> in 1900, found a difference of 400 per cent. in the activity of some fluidextracts. Fränkel<sup>5</sup> found variations of 300 to 400 per cent. in tincture and infusions. Edmunds,<sup>6</sup> in 1907, tested 17 commercial tinctures and found a variation of 400 per cent.

Many other similar results have been recorded, in some cases the reason being assigned to climate, soil, variety, or the locality from which the leaves were obtained.

Focke<sup>7</sup> observed that wild digitalis is more toxic than the cultivated and the second year's growth than the first. He also observed that the leaves gathered at seeding time are less active than when collected earlier. He was the first to record his observations as to the causes of deterioration and the effect of light and heat in drying the leaves. The former is negligible, but he considered that when dried in the air in the ordinary way without special care in preserving the activity is soon largely lost. This is considered to be due to the moisture content, which permitted the enzymes and ferments of the leaves to remain in an active state, and to their action in breaking down the sensitive glucosides to less active substances. His remedy is to heat the leaves rapidly to a temperature not to exceed 100°, drying to a moisture content of about ½ per cent. and preserving in dark air-tight jars.

Tordes,<sup>8</sup> in 1867, claimed that digitalis from the vicinity of Strassburg was better than that from other localities because of the careful selection, drying and preserving of the leaves. They used leaves of the second year's growth only, first dried in the shade, then in an oven at a temperature not over 40°. They were then kept in tin or glass containers away from light or moisture.

Sharp and Lancaster,<sup>9</sup> in a series of careful experiments, showed that digitalis leaves, not specially dried but kept dry, retained their activity for 11 years, while the fluid preparations began to deteriorate between the thirteenth and fifteenth months. They also observed that leaves of first-year plants were intensely bitter and probably very active.

<sup>4</sup> Bührer, Inaug. Diss., Basel, 1900.

<sup>5</sup> Fränkel, *Therap. Gegenw.*, 43, 106, 1902.

<sup>6</sup> Edmunds, *J. Am. Med. Assoc.*, 48, 1744, 1907.

<sup>7</sup> Focke, *Arch. Pharm.*, 245, 646, 1907.

<sup>8</sup> Tordes, *Gaz. Med. Strassburg*, 27, 191, 1867.

<sup>9</sup> Sharp and Lancaster, *Pharm. J.*, 32, 102, 1911.

Hatcher and Eggleston<sup>10</sup> found that old samples of digitalis leaves and tinctures, neither of them specially preserved, were not much below their original activity. They concluded that fluid preparations containing not less than 50 per cent. alcohol do not deteriorate to any considerable degree. This, however, is not in accord with most investigators, although the higher strengths of alcohol are in general much better for preserving the activity.

Houghton and Hamilton,<sup>11</sup> in a series of tests and retests of digitalis extracts, showed that none of them is free from the fault of deterioration, their results pointing to the apparent fact that the higher percentages of alcohol not only more completely extract but also more thoroughly preserve the active principles.

On the supposition that the strong alcohol destroys the active ferments these results are in accord with the results of Perrot and Goris,<sup>12</sup> who published a method by which the enzymes could be destroyed with the subsequent complete preservative of the drug in its original activity. This was accomplished by subjecting the drug to the vapors of boiling alcohol after which it was dried in the air. Such precautions, however, seem unnecessary in view of the results with old samples of digitalis obtained by the different investigators quoted, especially Hatcher, who found high values in 25-year-old leaves, and Sharp and Lancaster, who found 11-year-old drug to have lost little of its activity.

The writer recently had occasion to extract and test a sample which had been in the possession of Northwestern University for twenty-five years. Its activity was fully 150 per cent. of that of the average drug at present obtainable.

Recently the subject of drying digitalis leaves has come up in connection with the samples of this drug grown wild in Oregon and submitted to the government for the Medical Department of the Army. It was stated that unless the drug was dried in an oven, at 75 to 90°, it was practically worthless.

This statement being so entirely at variance with the opinions commonly held, some experiments were inaugurated to demonstrate its correctness. Unfortunately, there was not available a sufficient amount of the growing digitalis leaves to make the experiments con-

<sup>10</sup> Hatcher and Eggleston, *Am. J. Pharm.*, 85, 203, 1913.

<sup>11</sup> Houghton and Hamilton, *ibid.*, 81, 461, 1909.

<sup>12</sup> Perrot and Goris, *Abs. in La Presse Medicale*, 17, 776, 1909.



clusive but the results are apparently of sufficient importance to be published.

From some previous experiments, unpublished, it has been observed that the fresh leaves extracted with 95 per cent. alcohol had a higher degree of activity than the average digitalis on the market and apparently the tincture, so prepared, was more active than that prepared from a part of the same lot of leaves dried before extraction.

The following experiments were, therefore, planned and carried out. Fresh leaves were gathered from the flowering and fruiting plants in July, divided into three equal amounts and extracted as follows:

First: Extracted immediately with 95 per cent. alcohol for the moistening and then with 70 per cent. alcohol to complete exhaustion.

Second: Dried in an oven at temperatures ranging between 75° and 90°, then extracted with 70 per cent. alcohol. The drying covered a period of about 5 hours.

Third: Dried in the air and partly in the sun over a period of 4 days, then extracted with 70 per cent. alcohol.

The tinctures were made to the same amount on the basis of the weight of the oven-dried lot, which was considerably less than that of the air-dried sample.

Only two lots of drug were available, one being the official variety *digitalis purpurea*, and the other a non-official variety.

The results of essays are as follows, the method of testing being the M. L. D. method originally applied by Houghton.<sup>13</sup> The correctness of the end result was in every case checked by examining the heart of the dead frog to determine whether death occurred with heart in systole—the characteristic position from digitalis poisoning.

These results coincide with those previously obtained in that the fresh drug has greater toxicity than the dried. The experiments also show that the high temperature employed in the oven caused a greater immediate deterioration than the slower drying at the season temperatures.

Further experiments are planned to demonstrate whether the oven-dried drug is more stable than the air-dried sample but this point could not be considered, as not sufficient leaves were available

<sup>13</sup> Houghton, *J. Am. Med. Assoc.*, 31, 959, 1898.

TABLE I.

DIGITALIS PURPUREA FROM A FLOWER GARDEN IN DETROIT.

Not Dried.			Oven Dried.			Sun } Dried. Air }		
Weight.	Dose.	Result.	Weight.	Dose.	Result.	Weight.	Dose.	Result.
22	0.004	Alive	16.5	0.010	Alive	19	0.010	Dead
22	5	"	10.5	0.012	Dead	19	0.012	"
22.5	6	"	16.5	0.015	"	19.5	0.015	"
22.5	7	"	14	0.020	"	20.5	0.018	"
23	8	Dead	13.5	0.025	"	20.5	0.022	"
23.5	0.0045	Alive	23	0.008	Dead	24	0.007	Alive
25	55	"	24	0.010	"	24.5	0.008	"
25	65	"	24	0.012	"	24.5	0.009	Dead
25	75	Dead	24	0.014	"	25	0.010	"
26	0.0090	"	24	0.016	"	26	0.011	"
27	0.0055	Alive	20	0.006	Alive	22	0.007	Alive
27	65	"	20	0.007	"	22.5	0.008	"
27.5	75	"	21	0.008	"	23	0.009	Dead
29.5	85	Dead	21	0.009	"	24	0.010	"
30	0.01	"	21	0.010	Dead	26	0.011	Alive
27	0.0070	Alive	24.5	0.008	Alive	25.5	0.008	Dead
29.5	75	"	25	0.009	Dead	25.5	0.009	"
29.5	75	"	25.5	0.010	Alive	26	0.010	"
30.5	80	Dead	25.5	0.011	Dead	26	0.011	"
33	80	"	25.5	0.012	"	26	0.012	"

Summarizing the above.

0.007 killed none of 3

0.008 killed 1 of 3

0.008 killed 1 of 3

0.0075 killed 1 of 4

0.009 killed 1 of 2

0.009 killed 3 of 3

0.008 killed 3 of 3

0.010 killed 2 of 4

0.010 killed 4 of 4

0.011 killed 1 of 1

0.011 killed 2 of 3

0.012 killed 3 of 3

0.012 killed 2 of 2

Activity ..... 153

100

133

H. T. U. .... 9+

6

8

M. L. D. .... 0.008

0.011

0.009

Activity in terms of

undried drug .... 100%

72

81

to make the experiment conclusive. Such experiments should be continued over a period not less than three years.

In further consideration of the previously mentioned criticism against the Oregon air-dried leaves it should be noted that the method of testing was also called in question. On this point, while there is wide divergence of opinion as to which of several methods shows the real value of the drug, there is quite general agreement on the frog as the test animal, and until clinical evidence is brought

forward to negative the results it is logical to assume that the death of the frog with heart in systole, or the stoppage of the heart in systole in one hour is a satisfactory measure of the activity of a digitalis preparation. Compared with the guinea-pig method of Reed and Vanderkleed<sup>14</sup> and the Hatcher cat method,<sup>15</sup> both of which are purely toxicity methods, the frog methods have the advantage that deaths from other than digitalis poisoning are eliminated and form no part of the record.

TABLE II.

DIGITALIS LEAVES NON-OFFICIAL FROM A GARDEN ON GROSSE ILE, MICH.

Not Dried.			Oven Dried.			Sun } Dried. Air }		
Weight.	Dose.	Result.	Weight.	Dose.	Result.	Weight.	Dose.	Result.
17	0.004	Dead	20	0.004	Dead	23.5	0.002	Alive
18.5	0.005	"	27	0.005	"	25	0.003	Dead
19.5	0.006	"	23.5	0.006	"	25	0.004	"
27.5	0.007	"	23.5	0.007	"	25.5	0.005	"
18	0.0010	Alive	21	0.0010	Alive	19.5	0.0010	Alive
19	0.0020	Dead	22	0.0020	"	20	0.0015	"
19	0.0030	"	22.5	0.0030	"	20.5	0.0020	"
19	0.0040	"	25	0.0040	"	21.5	0.0025	"
20	0.0050	"	27.5	0.0050	Dead	22.5	0.0030	"
18	0.0010	Alive	23	0.0035	Dead	30	0.0025	Alive
19.5	0.0015	Dead	23	0.0040	"	28	0.0030	Dead
20.5	0.0020	"	23	0.0045	"	28	0.0035	"
21	0.0025	"	23.5	0.0050	"	29	0.0040	"
21	0.0030	"	23.5	0.0060	"	30	0.0045	"
			22.5	0.0020	Alive			
			23	0.0025	"			
			25	0.0030	"			
			27	0.0033	Dead			
			27.5	0.0040	"			

M. L. D. ....	0.0015	0.0035	0.0030
H. T. U. ....	44	19	22
Per cent. activity ..	730	310	370
Activity compared to undried .....	100%	42	50

One may conclude, therefore, that oven drying has no advantage over a reasonably rapid air drying of digitalis leaves, and that the drying causes a marked deterioration, no products more highly toxic

<sup>14</sup> Reed and Vanderkleed, *Am. J. Pharm.*, 80, 110, 1908.

<sup>15</sup> Hatcher and Brody, *ibid.*, 82, 369, 1910.



than those present in the crude drug having been developed during the process of drying.

RESEARCH LABORATORY, PARKE, DAVIS & Co.,  
DETROIT, MICH.

## MELTING POINT OF ROSIN.<sup>1</sup>

BY T. LINSEY CROSSLEY.

Certain large buyers of rosin have recently specified a melting point limit for this material. Samples have been submitted for this test, but without specifying how the test was to be carried out.

Properly speaking, rosin, like asphalt, has no definite melting point, therefore, any specification aiming to grade it by reference to its behavior on heating should state the method for obtaining results.

Schwalbe and Kuderlinn<sup>2</sup> not only state melting points, but record results to fractions of one degree and claim to differentiate between certain rosins by their melting points.

Several methods have been used to determine the quality of rosin as indicated by its action on heating. The closed capillary tube, of such general application, is used largely but, unless conditions of heating and observation are closely controlled, results are not uniform with different operators.

The following results were obtained on the same four samples by methods indicated:

Rosin.	$\frac{1}{4}$ " Column, ° F.	$\frac{1}{8}$ " Column, ° F.	Film, ° F.	Capillary, ° F.
1.....	174-184	169-172	150	146
	172-183	169-172	146	145
	.....	165-173	...	154 <sup>3</sup>
2.....	176-187	174-182	147	154
	174-185	167-176	155	147
	.....	.....	156	153
3.....	161-167	149-151	120 <sup>4</sup>	128
	161-157	145-146	134	130
	.....	.....	126	...
4.....	153-155	145-147	135	138
	147-155	144-145	133	136
	149-153	.....	...	...

<sup>1</sup> Reprinted from the *Jour. of Indust. and Engr. Chem.*, January, 1919.

<sup>2</sup> "Rosin Studies," *J. Soc. Chem. Ind.*, 30, 1397.

<sup>3</sup> Heated until clear.

<sup>4</sup> Probably mechanical weakness of film.

The first three methods were carried out as follows: Glass tubes of about  $\frac{3}{16}$  in. inside diameter and 2 in. long were prepared. These were dipped in melted rosin so that on cooling there was left inside the tube a column of rosin of the required depth. In the case of the method marked "film" the foot of the glass tube was heated slightly and applied carefully to the surface of the molten rosin so that upon cooling a thin film only of the rosin was formed. The tubes were attached to the thermometer in such a way that the bottom of the tube with the rosin was located about the center of the mercury bulb. The thermometer with tube attached was immersed in cold water in a 400 Cc. beaker with the bottom of the rosin column 1 in. below the surface. The temperature was raised about 3° per minute.

In the cases of  $\frac{1}{4}$  in. and  $\frac{1}{8}$  in. columns, it will be noted that two temperatures are given. The lower temperature indicates the point at which the rosin is soft enough for the water to enter the tube, the other being the point at which the water breaks through. The result is of course merely the point at which the viscosity is so reduced that it is overcome by the pressure of 1 in. of water. It is necessary that the heating should be well regulated. If heat is applied too rapidly it will naturally result in a higher final temperature and a wider spread between the two points.

The capillary tube method was carried out as follows: Tubes about 1 Mm. in diameter were prepared and sealed at one end. The rosin was pulverized between two pieces of paper. About 2 Cm. of the tube were filled with the powder, and it was attached to the thermometer as in the other cases, being also immersed in cold water and heated as before.

A reading glass was used to observe the result and the point at which the particles coalesced was noted as the melting point. It was not found advisable to carry the heating until the whole of the rosin in the tube became clear as this increased the range of personal error. There was found to be a more definite indication and closer agreement when the point of coalescence was noted.

The results obtained by the "film" method are for practical purposes the same as those obtained by the "capillary" method, but the tests are prepared more rapidly and with much less trouble, especially in the hands of unskilled assistants. The end-point is definitely established by the penetration of the water.

In all of these tests recently boiled water should be used, otherwise the rising bubbles of dissolved gases interfere in several days.

43 SCOTT STREET,  
TORONTO, CANADA.

## CORRESPONDENCE.

### THE COMMITTEE OF REVISION OF THE UNITED STATES PHARMACOPŒIA 1910-1920.

#### THE NEXT PHARMACOPŒIA.

May, 1920, only a little more than a year hence, will again witness the assembling in Washington of the delegates to the United States Pharmacopœial Convention. This fact should stimulate pre-convention activity on the part of those who have had experience with the present revision and are prepared to suggest improvements for a new edition.

It is desirable at this time that pharmacists, physicians, chemists, botanists, biological experts, or any others who use the U. S. P. IX. should submit to the chairman of the Revision Committee either personally or through associations, such helpful information as their experience may have suggested, or which may have come to their attention.

These suggestions will be compiled systematically and circularized to the present Revision Committee, the authors being credited in each instance with the recommendations, and the compilation will be submitted to the 1920 convention for the benefit of the new Committee of Revision.

You are earnestly urged to coöperate with the Committee of Revision in the preparation of this report and it is requested that in sending in your suggestions, the special form enclosed be employed. Please use a *separate sheet for each subject*. As many forms as are desired will be mailed on request.

Respectfully submitted,

CHARLES H. LAWALL,

*Chairman of the Committee of Revision of the United States  
Pharmacopœia.*



## UNITED STATES PHARMACOPŒIA.

*Suggestions for the U. S. P. X.*

(Use a separate sheet for each subject: additional sheets may be obtained from the chairman, Charles H. LaWall, 39 S. Tenth Street, Philadelphia, Pa.)

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*Subject Discussed* .....

*Brief Abstract of Recommendation* .....

*Details* .....

*Reasons for Proposal* .....

*Date* .....

Signature .....

Address .....

CONCERNING THE INFLUENCE OF STEMS AND ROOTS  
UPON THE ALKALOIDAL CONTENT OF  
STRAMONIUM.

New York, N. Y., Feb. 18, 1919.

DR. GEO. P. KOCH,  
Care of H. K. Mulford Co.,  
Glenolden, Pa.

*Dear Sir:* I found your article in the AMERICAN JOURNAL OF PHARMACY, January, 1919, on the alkaloidal content of stems, roots and leaves of stramonium quite interesting and instructive.

I would be glad to have a little further information regarding the samples identified as 223-4 and 5. I would assume from the statements on page 13 that these represent composites of samples nos. 211-12 and 13 with 10 per cent. of samples nos. 214-15 and 16. It is at once evident, however, that my understanding is not correct or that there has been a misprint.

If 10 per cent. of samples nos. 214-15 and 16 were added to samples nos. 211-12 and 13 in the order indicated, the resulting mixtures would assay approximately 0.55, 0.56 and 0.40.

I note that you refer to the 10 per cent. foreign material as "inert." It occurs to me, therefore, that possibly primary stems instead of secondary stems as stated was the material used, as this is relatively inert, while the secondary stems, as you have shown, could not be considered "inert" in comparison with the leaves.

It is possible that other readers may have found the same difficulty that I have found and possibly publication of the explanation would be found useful by others as well as myself.

Respectfully,

A. G. MURRAY,  
*Assistant Chemist.*

February 24, 1919.

DR. A. G. MURRAY,  
Room 1034, U. S. Appraiser's Stores,  
Christopher and Washington Sts.,  
New York City, N. Y.

*Dear Sir:* I have your letter of the 18th instant, relative to my paper on stramonium, which appeared in the January issue of the AMERICAN JOURNAL OF PHARMACY.

Samples were made by adding to the dry unground secondary stems, nos. 214, 215 and 216 to samples of dry leaves, nos. 211, 212 and 213, respectively, so that the former furnished 10 per cent. and the latter, 90 per cent. of the whole. These samples were made when the materials were in the *whole* condition, that is, before being ground for analysis. It is true, if 10 per cent. of the ground samples of nos. 214, 215 and 216 was added to nos. 211, 212 and 213, respectively, the resulting mixtures should certainly have assayed approximately, 0.55, 0.56 and 0.40 per cent., respectively, as you suggest. However, in making samples using the pieces of stems in the unground condition as before mentioned, due to the natural variation of the individual parts of the plants, it would be quite impossible to expect the analytical results to be as mathematically calculated. I must attribute the variation of these results to this fact of the variation of the individual parts of the plants, since the whole (unground parts) of these samples were mixed, then ground and mixed well for analysis.

In carrying out this experiment, it was not my intention to test the analytical method, but make mixtures of unground parts of the plants as nearly as possible as they would occur under practical

conditions, and find out if the mixtures were still fulfilling the United States Pharmacopœia requirement with regard to strength.

With reference to the 10 per cent. foreign material which was employed—10 per cent. of secondary stems were used as shown in the text of the article on page 13, line 16. My purpose in taking 10 per cent. of secondary stems was again for a practical consideration. If stems are considered foreign material by the United States Pharmacopœia in harvesting by picking the leaves or cutting the upper parts of the plant with a knife, we would be more apt to gather the secondary stems in conjunction with the leaf, than the primary stems.

It is true, from the results of the determinations as presented in table IV., page 14 of the article, secondary stems could hardly be considered "inert," or foreign material either, for that matter.

Regarding the accuracy of preparing the samples and the work in grinding the samples for analysis, and making the analytical determinations, very great care was manifested in every phase of the work. The analytical work was checked gravimetrically and volumetrically.

I am very glad that this matter has been called to my attention and your letter and a copy of my reply will be placed in the hands of the publishers as you suggested.

Very truly yours,

GEORGE P. KOCH,  
*Agricultural Chemist.*

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## COLLEGE NOTES.

FIRST NAVAL HOSPITAL UNIT AT P. C. P. CLOSING ITS WORK.—On Thursday evening, February 13, there was held in the Auditorium and Museum of the college the closing exercises of the U. S. Naval Hospital Corpsmen who had completed a three months' course of intensive training in the U. S. Naval Hospital Corps Training School of the Philadelphia College of Pharmacy.

Addresses were made by Admiral Hughes, Commandant of the Philadelphia Navy Yard and Ex-Governor Edwin S. Stuart.

One hundred and sixty-two men were in the unit at its beginning, but a number had been transferred or discharged during the three months. Certificates were awarded to the men who had satis-



factorily completed the course which comprised the fundamentals of pharmacy, chemistry, microscopy, first aid and instruction in typewriting given on two evenings of each week at the Peirce School.

It has been planned by the Navy Department to follow the first unit immediately by a second group of one hundred and fifteen men who will take a three or four months' special course.

THE P. C. P. IN THE MILITARY SERVICE.—The termination of the war found more than 500 students and alumni of the college wearing khaki uniforms. Eighteen are known to have laid down their lives on the altar of liberty and the first American enlisted man to die on "Flanders Fields" was Kenneth B. Hay, who at the time of his enlistment was a junior student at the college.

Dr. John A. Roddy, professor of bacteriology, is now a major in the medical service of the army, and is stationed in Oklahoma.

Mr. Ralph Foran has received his honorable discharge from the Chemical Warfare Service of the army and has returned to the college and resumed the position of assistant in the Analytical Chemical Laboratory.

Prof. Robert P. Fischelis, having been released from the Gas Warfare Service, has taken up his duties with Messrs. H. K. Mulford Company and resumed his lectures at the college.

Mr. Donald Margerum, a graduate of the Course in Food and Drug Chemistry at the college, and formerly an assistant to Prof. Charles H. LaWall in his private chemical laboratory, is now bacteriologist in a debarkation camp in Virginia.

Mr. Leon Claire, a member of the class of 1917, was officially cited for "conspicuous bravery" while serving as an ambulance driver in the Italian-Alpine section. He was trained at the famous Allentown, Pa., ambulance encampment. His brother, Captain Fred Claire, who had also attended the college for a short time, was one of the first American medical officers to lose his life at the front.

When the "Haverford" docked at the Port of Philadelphia, the

only returning Philadelphia soldier was W. Seimon, a graduate of the class of 1911, who volunteered early in the war and had seen active service abroad for over a year.

The college is preparing to do its share in helping discharged soldiers and sailors to locate themselves in the drug business or in some other civilian line of activity. A committee of the college under the chairmanship of Prof. Freeman P. Stroup is actively engaged in this service.

It has been proposed that the Philadelphia College of Pharmacy shall present to each student and alumnus who has served in the army or navy in the World War a suitably designed bronze medal as an evidence of appreciation for his services in behalf of the nation and as a token of honor and distinction.

"THE CORN EXCHANGE" COMMENDS THE COLLEGE.—*The Corn Exchange*, a magazine published by the Corn Exchange National Bank of Philadelphia, which has more than a local circulation, recently published a well-written article on the history of the Philadelphia College of Pharmacy and its record of achievements.

PROF. ROBERT P. FISCHELIS LECTURES ON GAS WARFARE.—Prof. Robert P. Fischelis has recently lectured before meetings of the New York Branch and the Philadelphia Branch of the American Pharmaceutical Association describing the methods of gas warfare and the problems, both offensive and defensive, which this had created. He also delivered a similar address before the Philadelphia Association of Credit Men at their recent meeting at the Ritz-Carlton Hotel.

# THE AMERICAN JOURNAL OF PHARMACY

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APRIL, 1919

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## EDITORIAL.

### THE EVIL OF DISPARAGEMENT.

The idealist, who by legitimate arguments and methods seeks to improve the practices of his vocation, deserves praise and encouragement. The higher his aim, the more ethical his purpose, the greater the possibility of a measure of success. He performs a service of value not alone to his chosen sphere of activity but also in that general advancement that we designate as the progress of the world.

The true idealist is naturally an optimist and, appreciating the value of the efforts of his predecessors, he predicates the advances that he advocates upon the foundations that they have established. By his very efforts in behalf of professional idealism, he evidences that he realizes that the goal is still in the distance and far ahead. The thinking observer is convinced that the desired purity of practice is not universally observed in any of the professions; that professional idealism is not now extant and that this is still an ethical *ignus fatuus*. The frailties of the human race and the perversities of human minds are continuously cropping out and attempting to demolish the work of the idealist. The several professions are cursed by their shysters, their quacks, and their hypocrites who shatter the ideals. The philosopher knows full well that all professional advancement will be the fruit resulting from the cultivation of the idealists.

In marked contrast to the services of the true idealist are the efforts of the false idealist, the disparager. He develops pessimism and with a deranged vision obstructing a view of the progress already made in his vocation, he endeavors to present his distorted picture and mental aberration to his associates. He may even hold



aloft the banner of professionalism while applying thereto the torch of disparagement.

Applying specifically our comments to the domain of pharmacy and especially American pharmacy, current literature demonstrates that it has become quite the fashion for a coterie of self-styled leaders who are possibly "rich in words and ideas but poor in the true knowledge and genuine studies," to continuously and deliberately "knock" pharmacy in print and in public utterances and some of the issues of "pharmaceutical journals" have been loaded down with disparagements of pharmacy.

Constructive criticism is always welcomed by those having at heart the welfare and progress of their vocation. There is, however, a wide difference between a "boost" and a "knock" and this is the fundamental difference between idealism and disparagement. It is manifestly unfair and unjust to lay at the door of pharmacy all of the pernicious results of that deep-rooted evil in the practice of the various branches of medicine, selfish commercialism. The service of the pharmacist being the last stage in the medical attention, it is influenced by the methods of practice in vogue by his predecessors. It is evident, that the commercial status of pharmacy, that is so energetically decried, results very largely from the existing commercialized practice of medicine. The encomiums of the professional status of the practice of medicine that are indulged in by some of the contributors to the pharmaceutical press are certainly not in harmony with the criticisms and deserved condemnations of medical practices published in recent issues of the *Journal of the American Medical Association*.

Let us recognize that "service is the base of all worthy enterprise." The pharmacist who conscientiously renders the service demanded of him by the community in which he is engaged and the status of the medical practice therein, is properly filling his responsibility to his profession and his duty to his fellow men.

Even a hasty review of the history of the development of pharmacy in America presents a long list of names of pharmacists who, notwithstanding their practical service with the mortar and pestle and graduate, have applied their minds and pens to the advancement of the profession of pharmacy and the construction of its literature, and of those active at the present time, many either are, or have been, engaged in the duties of the apothecary. American pharmacy has no need to apologize for its professional evolution.

It is doubtful if the authors of disparagements often give any thought whatever to the influence of their adverse criticisms. Their reflections are not very creditable to the teachers in the pharmacy schools who for several generations gave their lives and services to the elevation of the profession nor to those of the present generation who are continuing their effort. How can pharmacists expect to gain the respect of others so long as pharmacists do not respect their own position in society? How can pharmacy hope for the dignity and recognition from the other professions when in its own societies and journals the claims to such are discredited? How many promising youths with laudable ambitions for professional careers have been driven from pharmacy by these disparagers? The importance of pharmacy to the nation has even been minimized before the departments of the government by unnecessary and uncalled for slurs.

No nation can exist for any length of time when the love of country and patriotism is destroyed. No municipality can develop into an industrial, commercial or educational city of importance where civic pride is lacking. Similarly no vocation, either trade or profession, can expect satisfactory, progressive elevation without pride in its accomplishments and whole souled support of its votaries. Pharmaceutical progress demands rational constructive criticism, a change in tack, and adherence to a chart devoid of disparagements.

G. M. B.

#### THE REVENUE BILL OF 1918.

After months of debate, discussion and conference the Revenue Act of 1918 was enacted by Congress and by Presidential approval became operative on February 25, 1919, and while some of its tax provisions are made operative at fixed dates thereafter the main feature, namely the income tax which again commits the Federal Government to an extensive system of direct taxation, is retroactive.

By amending the title of the Bill by the addition of the phrase "and for other purposes" Congress legalized the introduction of radical legislation entirely foreign to the main purpose of the measure. The question of prohibition, with its recurring battles between the "wets" and the "drys" should have been fought out in some other way than by the introduction of "jokers" and questionable legislation in such an important measure as the main revenue law.

Likewise, was it a vicious and unfortunate piece of legislation to introduce therein amendments to the Harrison Anti-Narcotic Act. Anti-narcotic legislation was never intended to produce revenue, but its purpose was and is to suppress the evil use of narcotics. This is purely a police duty and the enforcement of such laws should be placed in the Department of Justice and not in the Treasury Department.

In the past, on several occasions, we have plainly presented in these columns the fact that "the Departments of the Government Need the Advice of the Drug Trade." The bill now commented upon, again very forcefully illustrates such need and some of the provisions now enacted, which are not very creditable to an intelligent law-creating body, could have been eliminated or corrected if Congress had not heedlessly refused to accept the suggestions and advice of men fully acquainted with conditions and the drug trade practices, whose services and counsel were proffered.

Following the erratic views shown in the revenue enactments of Congress, the drug trade has again been singled out for special taxation and the products usually sold by the drug trade, not excluding needed medicines and the ingredients thereof, bear a heavy burden of taxes. Consequently the druggists must become acquainted with those provisions of the Act that relate especially to the articles that enter into their dealings. This is going to be a difficult task for the drug trade, and the more one studies the ambiguous language of the sections relating to these matters the more numerous become the uncertainties and the questions as to the proper actions under the law.

The interpretation of the law has been largely left to the officials of the Bureau of Internal Revenue and they have the grave responsibility of framing regulations for the administration of a law the language of which in many parts is so involved that the very intent of the law-making body is in doubt. With the most painstaking and conscientious efforts on the part of officials and merchants alike there will remain numerous pitfalls and innumerable possibilities for errors and misunderstandings.

The collectors of internal revenue of the various districts have issued notices calling attention to the provisions of paragraph 12, section 1001, which provides that persons carrying on any of the branches of the liquor business named, including the *retail liquor dealer*, under which class many of the retail druggists by the neces-



sity of complying with the revenue laws were registered, would be required in prohibition localities to pay a special tax of \$1,000 and that "this section will prohibit the filling of prescriptions of distilled spirits in such territories unless \$1,000 tax is paid." It would have been equally appropriate for these collectors to have added, that the payment of the \$1,000 did "not exempt any person from any penalty or punishment provided by the laws of the states, territories or municipalities," or "authorize the commencement or continuation of any business contrary to such laws." This is one of the "jokers" introduced in the bill in the prohibition struggle and it is inconceivable that the ethical practice of medicine and pharmacy should be interfered with by such impractical legislation, and that professional efforts to conserve life and health could be so "juggled" by radical extremists with congressional sanction. It behooves the medical and pharmaceutical societies conjointly to see that in all state laws and municipal ordinances there is incorporated a properly worded exemption clause that will permit of the prescribing and dispensing of distilled spirits and wines in the legitimate exercise of their professional services.

Section 630 provides that after May 1, 1919, there shall be paid by the purchaser to the vendor at the time of sale, one cent for each ten cents or fraction thereof paid for any soft drink, ice-cream, ice-cream soda, sundae, or similar article of food and drink. The wording of this section, simple as the subject may appear, opens up at least two questions that may require official decisions and regulations to be promulgated. The wording of the section reads "when any of the above are sold on or after such date for consumption in or in proximity to such place of business." It would thus appear that if the *sale* is made prior to May 1, 1919, the *delivery* may be made at any subsequent time and be exempt from payment of the tax. Moreover, the tax need not be paid if the article is consumed elsewhere than on the premises of the vendor or in proximity thereto. Presumably the tax was to be levied upon this class of articles as luxuries and they cease to be such luxuries if bought and paid for in April or if consumed elsewhere than at the place of purchase. That such a ridiculous extension of the definition of a luxury, that such a gem of crudity, should be incorporated in an act of the United States Congress is as mortifying as ludicrous.

The drug trade had quite generally assumed that the tax on perfumes, toilet articles, etc., and on proprietary medicines was to be

a straight four per cent. tax on the wholesale price of these commodities instead of the two per cent. tax provided by the previous revenue bill, and that this was to be payable by the producer as heretofore in monthly reports. Section 907 of the Act, however, presents the possibility of an entirely different construction and a radical change not only in the rate of the tax to be paid on such articles when *sold on or after May 1, 1919, for consumption or use.* but also in method of payment. The tax to be imposed is "1 cent for each 25 cents or fraction thereof of the amount paid."

The method of collecting the tax imposed by this section is left to the judgment of the Commissioner and he is empowered to select either the collection "(1) *by stamp affixed to such article by the vendor, the cost of which shall be reimbursed to the vendor by the purchaser; or (2) by payment to the vendor by the purchaser at the time of the sale,* the taxes so collected being returned and paid to the United States by such vendor in the same manner as provided in section 502" (monthly returns under oath and in duplicate). The information available at present, is that the construction placed upon this section by the Department is that it is intended to be "a consumption" tax and *shall be paid by the purchaser.* The Canadian system of taxing proprietaries appears to have been in mind, and it is most likely that this tax will be collected by the affixing of a special stamp. The rate will be four per cent. on articles selling for 25 cents or more and ten per cent. on those selling for 10 cents and twenty per cent. on those selling for 5 cents. Under these conditions the salvation of the druggist or other vendor of such commodities will be in strict adherence to the intent of the law to make this a "consumer's tax," and to affix the stamp and collect the price from the purchaser with each sale.

It is to be noted that paragraph 2, relating to proprietary medicines, which are named by class designations, distinctly states that serums and anti-toxins are not to be included with the articles taxed as proprietaries. This is in conformity with a recent decision of the Commissioner of Internal Revenue, Daniel C. Roper, that vaccines, serums and similar biological products were not intended to be taxed under the revenue law of 1917, and the same decision will undoubtedly follow regarding the present law.

It is also noteworthy that toilet soaps and toilet soap powders have been excluded from the toilet articles, perfumes, etc., taxed under this section, and have been named in Section 900 under the

special tax of 3 per centum of the price at which they are sold by the manufacturer. It is assumed that under the title of toilet soaps and toilet soap powders will be included shaving soaps and shaving soap creams, and on these the tax will most likely be "absorbed" by the manufacturers or at least paid at the source of production.

The most vexing questions to the drug interests are presented by the vague and uncertain language of Sections 1006 and 1007, amending Sections 1 and 6 of the Act of Congress approved December 17, 1914, commonly known as the Harrison Act. These amendments well illustrate the viciousness of riders and the danger of permitting the extremist or over-zealous legislator to formulate radical amendments to existing laws. The attempt to strengthen the Harrison Act has resulted in increased confusion and difficulties to the Department as well as to the drug trade and medical practitioners. The re-licensing of those already licensed to act as manufacturers or distributors of opium, etc., until June 30, 1919, under an increased license fee, cannot be looked upon as necessary as a means of raising any additional revenue. The making of an additional inventory of the stocks on hand has been somewhat of a burden as well as a nuisance to these licensed distributors.

The attempt to classify the various dealers or distributors of the narcotics covered by the act by means of definitions has created some questions that will be exceedingly difficult for the Department to decide. The attempt has been to classify these as importers or manufacturers who shall pay \$24 per annum, wholesale dealers \$12, retail dealers \$6, and medical practitioners who shall pay \$3 per annum.

The definition for the first class named is "every person who imports, manufactures, compounds, or otherwise produces for sale or distribution any of the aforesaid drugs shall be deemed to be an importer, manufacturer or distributor." The bone of contention here is the meaning of the word "compounds" in the act. If the construction placed upon this be such as to cover the preparation of such medicines as paregoric, Bateman's drops or Brown mixture because opium in some form enter into these, then every person who manufactures such necessary pharmaceuticals becomes a compounder and subject to such tax as well as in any other class under which he may have to register.

The definition for a wholesale dealer is that "every person who sells or offers for sale any of said drugs in the original stamped



packages as hereinafter provided shall be deemed a wholesale dealer." Here again arises a serious question, as under the stamping provision every unit must be stamped and if the retailer sells on a prescription a tube of hypodermic or other tablets containing for example, morphine, in the original package or vial, which as a trade unit must be stamped, does he not become a wholesale dealer and subject to license as such?

The definition for a retail dealer is likewise somewhat involved as "every person who sells or dispenses from an original stamped package is deemed to be a retail dealer." As a physician must necessarily buy such articles as hypodermic tablets or other medicines containing any of these narcotics in stamped packages, does he not also become a retail dealer when he uses or dispenses same from these containers as under the law he must do? Will he have to be licensed under both classifications—physician and retail dealer?

The law provides that "there shall be collected a tax of one cent per ounce and any fraction of an ounce to be taxed as an ounce, the tax to be collected by an appropriate stamp affixed to the bottle or other container so as to securely seal the stopper, cover or wrapper thereto." Further that "it shall be unlawful for any person to purchase, sell, dispense or distribute any of these drugs except in the original stamped package, or from the original stamped package." The stamp is to be affixed by the importer, manufacturer, producer or compounder of the drug or preparation and so becomes a "manufacturers or 'producers' tax" and not a tax to be paid by a wholesaler or retailer on stock in hand.

A preliminary notice issued by some of the district collectors advising wholesale dealers, retail dealers, practitioners, etc., to affix these narcotic stamps to stock on hand was an error.

The wording of this section would appear to substantiate the opinion that this tax must be paid upon the ounce of the preparation, irrespective of the narcotic content.

The amended Section 6 of the Harrison Act permits the manufacturers and dealers in the articles exempted under the provisions of this section to register and procure narcotic supplies for such purpose by paying a tax of \$1.00 per year; thus covering the manufacturers of this class of exempted articles who were not included with those licensed under the original Harrison Act. The retail drug trade, as well as other dealers, including dispensing physicians should note that the amended section now requires that a record

shall be kept of all sales, exchanges or giving away of such preparations and in such a manner as the Commissioner of Internal Revenue shall direct. Doubtless, in due time the form of this record will be prescribed. In the meantime such sales or dispensing should be recorded.

It is evident that in carrying out the tax stamp provisions that the same importation of opium, morphine, etc., may be repeatedly taxed as it passes through the hands of the importer and manufacturer before it finally reaches the dealer in the form of finished preparation, as in each subdivision of package or change of product, restamping will undoubtedly be insisted upon.

The difficulties of administering the law as it now stands and the innumerable questions which are bound to arise regarding the purport of the wording will probably necessitate further reconsideration and further amendment of the Harrison Act.

G. M. B.

#### TREASURY DECISION NO. 2788.

Under date of February 6, 1919, Commissioner of Internal Revenue D. S. Roper issued T. D. 2788 relating to Nonbeverage distilled spirits and wines, being "Instructions relative to the sale and use of distilled spirits and wines for other than beverage purposes under the food control act of August 10, 1917, and the acts of November 21, 1918, and October 3, 1917." As these have a direct bearing upon the necessary work of pharmacists they should be studied by them so that they may be complied with if at all practicable.

There are unfortunately a number of statements and departmental rulings in this promulgation that we are compelled to criticize as contrary to the intent of the laws themselves and as unnecessary interferences with the legitimate practice of medicine and pharmacy.

The food conservation act of August 10, 1917, forbid the use of food materials in the production of distilled spirits *for beverage purposes* and provided that under such rules, regulations and bonds as the President may prescribe, such materials may be used for the production of distilled spirits exclusively *for other than beverage purposes*.

The act of November 21, 1918, reaffirmed this attitude of the government and provided: "The Commissioner of Internal Revenue

is hereby authorized and *directed to prescribe rules and regulations*, subject to the approval of the Secretary of the Treasury, in regard to the manufacture and sale of distilled spirits and removal of distilled spirits held in bond after June thirtieth, nineteen hundred and nineteen, until this act shall cease to operate, *for other than beverage purposes*; also in regard to the manufacture, sale, and *distribution of wine for sacramental, medicinal, or other than beverage uses.*"

The italicized portions as well as the context of these quotations, make it clear that the intent of Congress was that distilled spirits and wines were to be available for medicinal purposes. It would also appear that Congress recognized the need of distilled spirits and wines in their *pure state as medicines* and there is nothing whatever in the wording that would indicate that these must be "denatured" so as to render them unfit for medicinal use per se.

The present regulations while modifying prior decisions only reaffirm the attitude that the Department had assumed that pure alcohol and other distilled spirits and pure wines cannot be prescribed or dispensed for medicinal use. This decision would make the procuring of such after June 30, 1919, impossible and illegal even on prescription and the regulations evidence the purpose to interfere with the legitimate practice of medicine and pharmacy despite the intent of Congress as shown by the wording of the acts.

It is hard to reconcile the power to legislate vested by the Constitution solely in Congress, with the assumed authority of the executive departments to abridge or abrogate the laws or modify their evident intent. The Food and Drugs Act named the Pharmacopœia of the United States and the National Formulary as the authority for the standards of quality and purity for drugs and defines the meaning of the word drug. That definition and the standards fixed by the authorities named, remain the law of the Country until rescinded by Congress itself. The U. S. Pharmacopœia accurately defines and describes the legal standard for alcohol and under the existing law, only alcohol of the U. S. P. standard can be sold or dispensed when the drug alcohol is ordered. The Internal Revenue Department by an edict now sets aside this authorized and legal standard and decrees that even "on a physician's prescription" U. S. P. Alcohol "must not be dispensed" unless first denatured (adulterated within the meaning of the Food and Drugs Act) by the addition of a foreign poisonous substance and labelled "Poison." Under this decision, the law enacted as the



means of preventing adulteration of drugs, must be continuously violated by acts contrary to the judgment of the physician and to the detriment of his patient, and the evident intent of Congress in these enactments nullified.

The Department has not been entirely consistent in this decision. While denying to the patient suffering with fever the right to be rubbed down with pure non-beverage alcohol of the pharmacopœial standard, even though such medication is directed by the attending physician, the regulations nevertheless permit that "nonbeverage distilled spirits may be used for rubbing purposes in Turkish bath establishments," providing no charge is made for alcohol used in rubbing the customer. The proprietor of such an establishment easily complies with the regulations by making his service charge sufficient to include the value of the alcohol. Which of these is the use, deserving first consideration as coming within the designation "medicinal"? Which is the most necessary? and the most humanitarian?

The regulations provide that "spirits of a potable proof which were entered into warehouses and marked and branded as whisky, rum, gin, brandy, etc., will be presumed to be for use for beverage purposes when withdrawn or sold. Here again the "presumed" position will preclude the use of these as "medicinal" agents and annul the apparent intent of the law, although many of our most able physicians continue to consider these distilled spirits valuable as medicines.

From time immemorial, wines have been used as remedial agents as well as for solvents and preservatives of other medicinal substances. The regulations assert that "It is not *believed* that there is any legitimate use for wines for medicinal purposes, and since it is impracticable to determine the exact purpose of use when taken internally, except when used for sacramental purposes, no wines, as such, may be sold for internal use on a physician's prescription or otherwise as medicines." The "belief" of some official temporarily in a position of authority to render a decision is set up in opposition to the belief of thousands of capable physicians that wines are at times very necessary as medicines. It is not an uncommon experience that the administration of small portions of champagne wine, when the stomach will retain nothing else, has tided over the crisis and saved the patient's life. But under the existing conditions, ex-

perience and medical knowledge are not to be given credence or weighed against departmental "*belief*."

Pharmacists and manufacturers may likewise have some difficulty to obtain the supplies of sherry or other wines needed for the manufacture of N.F. preparations and other standard formulas calling for wine as an ingredient. In the National Formulary we have upwards of a score of such formulas and the question confronting the Committee on N.F. and the pharmacists of the country is what changes may have to be made in these legal standards to comply with this irrational contravention and then a subsequent annoyance will be the explanations that may have to be made to customers and law officers of the deviations from the official formulas.

The homeopathic physicians are far from contented with the regulation "that a homeopathic physician or any other person may obtain from the pharmacist not exceeding 2 drachms of any attenuation, potency, or dilution at one time without filing bond or obtaining permit."

The question of solving the evil of intemperance can surely be attained by sane laws and regulations that will not interfere with legitimate medicinal practice and thereby imperil the lives of many of our people. Impractical and radical regulations may result in a reversion of public sentiment to such an extent as to actually defeat the purpose of the prohibitionists.

G. M. B.

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PRIVATE—SECRET—PERSONAL—NO. 1.<sup>1</sup>

"Come, now, and let us reason together!"

BY JOHN URI LLOYD, PHAR.M.

In the opinion of this writer, misunderstanding of ideals and motives causes much of the trouble that prevails when, in anger, friend parts from friend. Neglect to define one's position properly and fully, on a problem that presents several viewpoints, may breed antagonisms where, could the two minds be brought together before prejudice was bred, harmony instead of discord would have resulted. Perhaps the misconception of the meaning of a word or words,

<sup>1</sup> Privilege of publication in a medical journal is extended the author.

where shades of distinction may perplex even an expert, holds men's minds apart. Comes first a one-sided impression, then, as discussion progresses, intensity of argumentative passion takes its place, next comes self-bred fanaticism in which the disputants forget the original cause, to make personal their grievances, which may finally lead to estrangement, even hatred, each of the other. Leaders may they now become of discordant factions, who jump at conclusions with not less vehemence than have their misled authorities. The perhaps obsolete meaning of a word may be the foundation on which one party stands,—the not less unimportant dictionary shading of that word's application may possess the other.

To meet together in friendly discussion of this or any other problem becomes now impossible,—individual hatred has made fanatics of one and all. Helpless to argument, as a fish in a net, is the man steeped in dogmatic fanaticism. Cast your eye about you, possibly the mote that rests therein may yet permit you to perceive the faults of others, who in turn see your mote as a mighty beam that obstructs your vision. To cast out these motes is as difficult as to take to one's self the time-honored text that heads this article,

“Come, now, and let us reason together!”

Many are the men deep-dyed in medical and pharmaceutical ethics, who during past decades delighted to bite and scratch and fight each other over the words “secret” and “private.” To many men involved in the ethics of medicine, as well as pharmacy, these words were from every angle alike discrediting. And yet, in some directions, this writer believes that neither word, properly considered, is subject to criticism when applied to either legitimate pharmacy or ethical medicine. Indeed, he has been so bold as to assert, for many years, that the very leaders in self-made ethics laid down for others to follow, might well, before assailing a neighbor, search their own eye for the mote which perhaps needs, for location, neither microscope nor telescope.

Take your dictionary. Observe how liberal is the expert lexicographer concerning the shadings of this word SECRET: “*hidden; concealed; not revealed; private*” (Webster). Note that in establishing its authoritative use, appropriate quotations are offered, from various authorities: “*secret* graces and virtues are the hidden beauties of a soul.” “A *secret* or silent prayer.” Now contrast this



implied altruistic use of the word, with "I will have nothing *under-hand*." Between these rests a line of shadings that nearly parallel, in their contact meanings, the questionings of a fungus expert perplexed in his art. And yet, in the ethics of some authorities in medicine, but one thought applies to him who practices any phase of therapeutic *secrecy*. He is not of the Code,—altogether bad, he is "*irregular*."

These years ago, this writer filled prescriptions for a talented physician, a regular of the regulars. In those days, oftener than now, the "*Code*" was used as an implement to distinguish between him outside the pale and him blessed by the code's all-wise protection. This physician stands yet in memory as a conscientious, gifted man, second to no other, professionally or ethically.

Consider now one of his patients, whose face rises to memory's call. Unconscious was she that, a hypochondriac, she was a representative of a peevish class. Medicine she *must* have, to live. To her, the (this) physician was next to the Infallible. And yet, time after time his prescriptions for her use were *bread pills*, dusted sometimes with cinnamon, again with licorice, and occasionally with wood ashes. Varied in size and color were they, to serve this lady's need, and well did they accomplish their purpose.

And yet, some there are who might argue that in comparison with deception such as this, quackery need not blush,—a problem each reader is entitled to settle to his own satisfaction. Another might assert that mind influence (cure) might justify its "cause" by this bread-pill example, a subject it is also unnecessary for us now to discuss.

Ask the physician of the olden time, whose patients would not take *calomel*, How many prescriptions of Hyd. Chlor. Mit. were written for these "fanatics." In those days, some persons believed that *quinine* "wracked the bones," and bred untold disorders. Cinchona, "the Jesuit's pernicious powder," was by some considered of the Devil's brew. Ask the physician of half a century ago how many prescriptions he wrote, for "Huxham's Tincture," where quinine would better have served their purpose?

In those days, it was the duty of the druggist to refrain from explaining to any layman the prescription's content. Is not this yet the proper rule? Did not this *secrecy* of the physician in his methods of prescription mysticism give rise to charges and innuendoes innumerable? Were not the very framers of the code against

secrecy in medicine, in the eyes of a great part of the public, the most pronounced of all secret practitioners? Did they not, in the opinion of many men, approach perilously near the "Black Art" in their use of cabalistic formulæ?

Do not accept that by citing these examples this writer makes an argument favoring the open door between physician and patient, in therapeutic agents. Instead, he believes that the physician should not be hampered by unqualified questioners. He should be implicitly trusted. He is called to treat our loved ones, because these patients cannot serve themselves. Never does this writer ask his physician the names of the remedies administered to a member of his family, or to himself.

The object of this phase of our discussion is to indicate that the term *secret* needs not, even with a physician, be always accepted in the sense some authorities might and do apply to it. The very province of the physician entitles him to the privilege of professional reserve that, for special service, even approaches deception, when the patient's welfare so demands. And, what of the pharmacist?

Knows anyone the pharmacist who to a physician's patient discloses the ingredients of a prescription? Instead, does he not ever sacrifice himself in financial directions to preserve inviolate the trust placed in him by the physician? Is he not constantly solicited to explain the prescription? Is not now, as fifty years ago, the answer: "Ask the doctor, I have no right to discuss the subject?" Does he not accept that *secrecy* as to some of the ingredients may be very necessary? Have we not examples of cases where the care of a physician as to overdoses was deplorably disturbed by patients who, getting the name of an ingredient, purchased the drug in bulk, to his distress? Behold we not today the evils of self-medication by him who purchases the fashionable synthetics that, in this writer's opinion, should be administered carefully, even by the physician who stands with his hand on the patient's pulse. Possibly greater *secrecy* might today be serviceable to humanity. Would it not be better had greater secrecy long since been practiced in some directions? Who knows the dire effects of some of the modern agents unwisely made familiar to the public? Well does this Nation comprehend the deplorable results of such as opium.

"Come, now, and let us reason together!" Concede that some forms of secrecy in therapeutics are closely akin to charlatanism, but that others may be necessary to the patient's comfort and welfare.

This leads us to a consideration of the word *private*, which is even more obnoxious to some persons involved in enforcing pharmacy ethics on their neighbors, than was the word *secret* to the "ethical purist" of the old-time medical code.

## SOME OBSERVATIONS ON THE USE OF BORIC ACID AS A DISINFECTANT.<sup>1</sup>

BY FRED. W. TANNER AND RUTH S. FUNK,

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Two general procedures are available for the prevention of premature death, building up the body resistance and the destruction of infective agents in man's environment. Among the procedures which may be used to reduce the possibility of infection from environment, is disinfection. Many different chemicals and reagents are used to destroy pathogenic microorganisms some of which are of undoubted value while others, even though they may have rather extended application, may hardly be comprehended as having much destructive action toward bacteria. Among such a class of disinfectants we might expect to find boric acid. With some practitioners this is regarded as an efficient bactericide since they recommend its use at such occasions as child-birth and other occasions where it has been proven that the bacterial flora must be controlled.

### HISTORICAL.

The literature is very extensive on the use of boric acid as a food preservative. Agulhon<sup>2</sup> found that boric acid solutions were not antiseptic. Bernstein<sup>3</sup> made a rather careful study of the use of this compound as a food preservative and secured some data which may be of interest in this connection. He reported a marked selective action on microorganisms inhibiting yeasts and members of

<sup>1</sup> From the Laboratories of Bacteriology of the University of Illinois, Urbana, Ill.

<sup>2</sup> Agulhon, Are Boric Acid Solutions Antiseptic, *Rev. mens. med. prat.*, 1912, 51.

<sup>3</sup> Bernstein, J., Preliminary Note on a New Aspect of the Effects of Boric Acid as a Food Preservative, *Brit. Med. Jour.*, No. 2572, 928-9.



the proteus group of bacteria. Members of the *B. coli* group were not affected. Strassburger<sup>4</sup> found the same selective action. This investigator states some organisms are able to stand large doses of boric acid with impunity while others find small doses very toxic. Agullion<sup>5</sup> found that this chemical in saturated solutions had little retarding effect on the activity of enzymes. E'we and Vanderkleed<sup>6</sup> have stated that two grains of boric acid would preserve a sample of urine for six days, whereas the control sample spoiled in three days. Kuehle<sup>7</sup> found that  $B_2O_3$  was a very feeble antiseptic and in no way had the ability to check undesirable bacterial change. Such are the impressions which one is able to get from the literature concerning this subject.

Ochsner<sup>8</sup> stated that this chemical did not destroy pathogenic bacteria but did diminish their virulence.

#### EXPERIMENTAL.

No attempt was made to carry out an exhaustive investigation on boric acid as a disinfectant. An attempt was made, however, to determine just how toxic a solution of boric acid was toward bacteria. To do this, a saturated solution in distilled water was used. Chemical handbooks state that such a solution of this acid approaches a 4 per cent. solution. Such solutions are generally used in disinfection.

The first experiment consisted in adding increasing amounts of boric acid to melted dextrose agar and allowing the tubes to harden in the slanted position. After that the slants were inoculated by streaking and incubated. The incubation period was four days at 37° C. after which the culture tubes were observed. The results with common bacteria are given in Table I. The signs used therein have the following values: ++ = normal growth determined from an untreated agar culture; + = growth; — = no growth.

<sup>4</sup> Strassburger, F., Boric Acid as a Preservative with Reference to Its Use in the preserving of Crabs, *Hyg. Rund.*, 19, 169-85.

<sup>5</sup> Agullion, H., The Influence of Boric Acid on the Action of Diastasic Ferments, *Ann. Past. Inst.*, 29, 495-518. *Chem. Absts.*, 5, 1911, 1788.

<sup>6</sup> E'we, G. E., and Vanderkleed, C. E., Boric Acid as a Preservative for Urine Analysis, *J. Amer. Pharm. Assoc.*, 2, 979-982.

<sup>7</sup> Kuehle, H., Boric Acid as a Preservative, *Pharm. Centr.*, 50, 559.

<sup>8</sup> Ochsner, E. H., The Biochemistry of Topical Applications with Special Reference to the Use of Boric Acid in Septic Infections, *Chemical Abstracts*, 12, 1918, 191.

An examination of this table seems to indicate very little if any germicidal action of the boric acid even when added to the agar in rather large amounts. *P. fluorescens liquefaciens* seemed to be

TABLE I.

Organism.	Number of Cubic Centimeters of Saturated Solution Boric Acid Added to Each Tube of Agar.									
	.1.	.2.	.3.	.4.	.5.	.6.	.7.	.8.	.9.	1 cc.
<i>B. arborescens</i> .....	—	—	—	—	—	—	—	—	—	—
<i>B. aërogenes</i> .....	++	++	+	+	+	+	+	+	—	—
<i>B. capsulatus</i> .....	++	++	+	+	+	+	+	+	+	±
<i>B. cereus</i> .....	±	±	—	—	—	—	—	—	—	—
<i>B. cloacæ</i> .....	++	++	+	+	+	+	+	±	±	±
<i>B. colon</i> .....	++	++	++	++	+	+	+	+	+	+
<i>B. cyanogenus</i> .....	++	+	+	+	—	—	—	—	—	—
<i>B. dysenteriae</i> .....	+	+	+	+	+	—	—	—	—	—
<i>B. enteritidis</i> (Gaertner) ...	++	++	++	+	+	+	+	+	+	+
<i>B. fluorescens liquefaciens</i> ..	+	+	+	—	—	—	—	—	—	—
<i>B. gasoformans</i> .....	++	++	++	++	+	+	+	+	+	—
<i>B. granulosum</i> .....	+	+	+	—	—	—	—	—	—	—
<i>B. of hog cholera</i> .....	++	++	++	++	++	+	—	—	—	—
<i>B. mesentericus</i> .....	++	++	++	+	+	—	—	—	—	—
<i>B. proteus vulgaris</i> .....	++	++	++	++	++	+	—	—	—	—
<i>Strep. byogenes</i> .....	++	++	++	++	++	+	+	+	+	+
<i>B. paratyphosus "A"</i> .....	++	++	+	++	+	±	±	±	±	—
<i>B. paratyphosus "B"</i> .....	++	++	+	+	+	+	—	—	—	—
<i>B. typhosus</i> .....	++	+	+	+	+	+	+	+	±	±
<i>B. pyocyaneus</i> .....	++	++	++	+	+	+	—	—	—	—

affected to the greater extent since it did not grow on agar slants with over 0.4 Cc. of saturated boric acid solution. A few other organisms as indicated in the table seemed to be inhibited when quantities of saturated boric acid solution approaching 1 Cc. were used. It is possible that a selective action may be secured when this reagent is added to agar.

In order to use a different environment and a fluid medium, the same experiment was repeated with Frankel's solution which had the following composition: 5 Gms. sodium chloride, 2 Gms. mono-calcium phosphate, 6 Cc. ammonium lactate, 4 Gms. asparagin, 1 liter distilled water, 20 Cc. *N* sodium hydroxide. To 5 Cc. of this solution were added increasing quantities of saturated boric acid solution after which the tubes were inoculated with pure cultures and incubated at 37° C., using in each case the same amount of inoculum. The results are shown in Table II.

From this table it is apparent that any inhibitory power possessed by boric acid is not constant. Little decrease in growth was

TABLE II.

Results—Organism.	Number of Cubic Centimeters of Saturated Solution of Boric Acid Added to 5 Cc. of Frankel's Solution.									
	.1.	.2.	.3.	.4.	.5.	.6.	.7.	.8.	.9.	1 Cc.
<i>B. arborescens</i> .....	+	+	+	—	—	—	—	—	—	—
<i>B. capsulatus</i> .....	++	++	++	++	++	++	+	+	—	—
<i>B. cereus</i> .....	++	++	++	+	+	+	—	—	—	—
<i>B. claoea</i> .....	++	++	++	+	+	+	+	+	+	+
<i>B. colon</i> .....	++	++	++	++	+	+	+	+	+	+
<i>B. dysenteriae</i> .....	++	++	++	++	+	+	+	—	—	—
<i>H. enteritidis</i> .....	++	++	+	+	+	+	+	+	+	+
<i>B. fluorescens liquefaciens</i> ..	++	+	+	+	+	+	+	—	—	—
<i>B. gasoformans</i> .....	++	++	+	+	+	+	+	+	+	+
<i>B. granulosum</i> .....	++	++	++	++	++	+	+	+	+	+
<i>B. of hog cholera</i> .....	++	++	+	+	+	—	—	—	—	—
<i>B. mesentericus</i> .....	++	++	++	++	+	+	+	—	—	—
<i>B. proteus vulgaris</i> .....	++	++	++	++	+	+	—	—	—	—
<i>P. pyocyaneus</i> .....	++	++	++	++	++	++	+	+	—	—
<i>Strep. pyogenes</i> .....	+	+	+	+	+	+	+	+	+	+
<i>B. paratyphosus</i> "A" .....	++	++	+	+	—	—	—	—	—	—
<i>B. paratyphosus</i> "B" .....	++	++	++	+	+	+	+	—	—	—
<i>B. typhosus</i> .....	++	++	+	+	+	—	—	—	—	—

secured until after 0.6 Cc. of the acid were added to 5 Cc. of Frankel's solution.

In order to use a larger amount of the boric acid, the silk thread method, which has been so serviceable in the past in similar studies, was used.

Sterile white silk threads one inch long were placed in broth suspension of the organism for 1½ hours. They were then re-

TABLE III.

Results—Organism.	Time in Minutes that a Silk Thread Impregnated with the Organism was Exposed to Saturated Boric Acid.									
	5.	10.	15.	20.	25.	30.	35.	40.	45.	50.
<i>B. arborescens</i> .....	++	++	++	++	++	++	++	++	++	++
<i>B. coli</i> .....	++	++	++	++	++	++	++	++	++	+
<i>B. enteritidis</i> .....	++	++	++	++	++	++	++	++	++	++
<i>B. typhosus</i> .....	++	++	++	++	++	++	—	—	—	—
<i>B. paratyphosus</i> "B" ..	++	++	++	++	++	++	++	++	++	++
<i>B. cereus</i> .....	++	++	++	++	++	++	++	++	++	++
<i>B. capsulatus</i> .....	+			+						=
<i>B. cyanogens</i> .....	++	++	++	++	++	++	++	++	++	+
<i>B. proteus vulgaris</i> ....	++	++	++	++	++	++	++	++	++	++

++ normal. + some growth. — no growth.

moved with a sterile platinum needle, placed into sterile Petri dishes and placed in 37° C. temperature room over night (ten



threads to each organism). Each thread was then placed in a saturated solution of boric acid and exposed, respectively, 5, 10, 15, 20, 25, 30, 35, 40, 45 and 50 minutes, after which each thread was placed in a tube of sterile plain broth and incubated at 37° C. for one week.

Controls were made for each organism by placing the dried thread (from the suspension) directly without exposure to boric acid, into tubes of plain broth.

A check was also made on the boric acid by placing one Cc. boric acid in a tube of plain broth and incubating at 37° C. The results of this experiment are shown in Table III.

Even under these conditions, boric acid exhibited very little inhibitive effect on bacteria. In this experiment the entire saturated solution was available for action toward the bacteria. A saturated solution of the boric acid when allowed to act on the organisms for 50 minutes did not kill them. *Bacillus typhosus* was killed by 35 minutes' exposure to the saturated boric acid.

An attempt was made to determine whether boric acid, acting as an antiseptic, would effect yeast fermentations. It seemed to possess no consistent action since in many cases more gas was formed after exposure to boric acid than before. Under the conditions of this experiment the boric acid seemed to have no antiseptic activity in reducing the zymogenic activity of the yeast.

*Conclusions.*—A prominent writer on preventive medicine has stated that boric acid was a "camouflage" disinfectant. Such seems to be the result of this short study. The use of this reagent in those cases where disinfection is absolutely essential, should be discontinued. It seems probable that many of the salts of boric acid may have as limited a disinfecting power as the acid itself. The statements of the vendors are possibly misleading.

## DIGITALIS PURPUREA.

BY GEORGE P. KOCH, PH.D., AND J. RUSSELL BUTLER.<sup>1</sup>

### INTRODUCTION.

The cultivation of digitalis in the United States, as in the case of belladonna and hyoscyamus, has resulted to a great extent from the European war. Since our principal source of supply was cut off, there naturally resulted a great advance in the price paid for digitalis leaves. Harvesting the large amount of digitalis which grew wild in the western part of Washington and Oregon and other states did not overstock the market. A considerable number of individuals attempted to grow digitalis on a commercial scale, but, due to inexperience with such a crop, there results the first few years were more or less failures. At present, however, growing digitalis has passed the experimental stage and a successful crop can be grown on a commercial scale. In those localities where these plants grow very luxuriantly under uncultivated (wild) conditions, it would require a comparatively small amount of attention to grow it commercially. To study digitalis so that a successful and paying crop can always be obtained in localities which are not so favorable for its growth, a number of experiments were made covering the most important phases of cultivation of this plant.

### STUDY OF THE GERMINATION OF DIGITALIS.

Viable digitalis seeds, as seeds of other medicinal plants, have been difficult to procure. This is principally due to the fact that in those localities of the United States where digitalis has been cultivated for commercial purposes, the winters are so severe that if the plant is to be grown as a biennial or perennial, the roots have to be removed from the soil in the late fall and stored under cover. This is a rather expensive undertaking, and has discouraged the growing of digitalis as a perennial plant.

The seeds of digitalis are very small and usually not very viable. Stockberger (14) states that they do not germinate very well except when under the very best cultural conditions. Newcomb (11) finds

<sup>1</sup> The authors are indebted to Dr. Paul S. Pittenger for having made the alkaloid determinations and take this opportunity to express their thanks in this connection.

that it requires from 9 to 15 days for digitalis to germinate. Borne-man (5) states that digitalis plants come through the ground in about 9 days and at the end of three weeks, will be ready for transplanting into pots or in plats.

To determine whether or not the blotting paper method of germinating seeds could be applied to testing the viability of digitalis and at the same time, to determine how long a period of time it requires for seed of digitalis to germinate, two samples of 100 seeds each were germinated between blotters.

. TABLE I.

SHOWING THE LENGTH OF TIME IT REQUIRES DIGITALIS SEED TO GERMINATE BETWEEN BLOTting PAPER.

Sampl No.	Percentage of Seeds Germinated.			
	4th Day.	5th Day.	7th Day.	9th Day.
1	76	78	84	87
2	76	79	84	86

With the above sample of digitalis seed, 86 per cent. germinated on the ninth day. It will be seen that very few more had germinated on the ninth day than on the seventh. This method of testing the viability of digitalis seed proved very successful. By applying it to four other samples of digitalis seed, it was found that these tested 91, 87, 42 and 7.5 per cent. It is apparent from these figures that there is a great variation in the viability of digitalis seed.

Digitalis seed planted on the soil were covered with a small layer of sand. Those were kept moist and to prevent excessive evaporation were covered with burlap. Most of the sprouts were out of the soil and were  $\frac{3}{4}$  inch high on the sixth day after planting.

#### STUDY OF THE PLANTING OF DIGITALIS.

What is the most satisfactory method of planting digitalis? Stockberger (14) says, "Sowing the seed directly in the field occasionally gives good results, but is so often unsuccessful that it can not be recommended." Miller (10) germinated digitalis seed in the greenhouse the first week in December, grew the plants in flats until the middle of March, after which time he put them in a cold frame until May when they were planted in the field. Borne-man (5) says that digitalis plants come through the ground in about



nine days. Three weeks after this period, they will be ready to transplant into pots or in flats. He states further, that after they have attained the height of about 6 inches, they will be ready for planting in the permanent bed. He recommends planting the plants 24 inches apart in the rows, and the rows three feet apart. Newcomb (11) after germinating the seeds, transplanted the plantlet in flats. They were grown until they were large enough to transplant into 2 to 2½ inch pots. Later, they were planted in the field.

With the high cost of labor in the United States, it is very evident that commercially, by employing the above method, we could not be very successful, unless a high price was received for dry digitalis leaves. To reduce the cost of production as much as possible, an idea of growing the plants directly in small pots was tried. One hundred 1¾ inch pots were filled with a light compact soil and then seeded with digitalis seeds. The seeds were covered with a light layer of sand. The pots were kept moist by watering carefully twice a day and to prevent excessive evaporation, were covered with burlap until the seed had germinated. The seed was sown on May 10, and on June 13 the plants were in fine condition. As there were from 6 to 15 plants in each pot, they were thinned out so that but 3 or 4 remained in each pot. This was a very easy task and required but little time as the whole mass of plants and soil were removed from the pot and this was divided into from 2 to 4 parts, depending upon the number of plants present. Two weeks after thinning out, the plants were large enough to plant in the field. At this period, they were about 2 inches high and planting the soil from the pot with the roots, left the roots intact and the plants grew at once when transplanted in the field. Hence, it will be seen that by the above method, three steps were required until the digitalis plants were finally in the field. This method having proved successful, it, with a few modifications, was employed in growing the commercial material. If a planter, such as a tobacco planter, is employed in transplanting the plants in the field, it is desirable to have the plants slightly larger than 2 inches. In 4 to 6 weeks after thinning out, such plants could be obtained.

Is it possible to secure a satisfactory crop by seeding digitalis seeds in the field directly? Experiments were made covering this factor. It was found that ordinarily the weed seeds germinated so readily that the digitalis plantlets were hard to find among the weeds. Were it possible to keep the plant beds entirely free from

weeds, seeding directly in the field would be a satisfactory method of procuring the plants.

#### EFFECT OF FERTILIZATION UPON THE GROWTH OF DIGITALIS.

Formerly there was considerable discussion concerning the relative alkaloidal activity of the wild and garden grown leaves of digitalis. Several investigators were of the opinion that digitalis grown wild in its natural habitat, had a higher activity than that which was cultivated. On this phase, Hall (6) concludes that there is not necessarily any difference in the activity of wild and garden grown digitalis. In determining the effect of various inorganic fertilizers upon digitalis, Miller (10) found no appreciable difference in the activity in plants which received fertilizers, and in the controls. With regard to digitalis seed bed, Borneman (5) states that the soil for seeding should be well prepared, having been limed and well mulched. Holm (7) says that fox gloves grew best in well drained loose soil, which is mixed with leaf mold, but it does not grow in calcareous soil.

TABLE II.

SHOWING THE EFFECT OF INORGANIC FERTILIZERS UPON THE GROWTH OF DIGITALIS IN A CLAY LOAM SOIL.

Fertilizer Application <sup>3</sup>	Wt. of Plants, Grs.	Average, Grs.
1. No fertilizer .....	7.0	
2. No fertilizer .....	8.5	7.7
3. Complete fertilizer .....	11.0	
4. Complete fertilizer .....	10.7	10.8
5. Complete fertilizer—Ca(H <sub>2</sub> PO <sub>4</sub> ) <sub>2</sub> ·2H <sub>2</sub> O ....	9.3	
6. Complete fertilizer—Ca(H <sub>2</sub> PO <sub>4</sub> ) <sub>2</sub> ·2H <sub>2</sub> O ....	10.3	9.8
7. Complete fertilizer—K <sub>2</sub> SO <sub>4</sub> .....	9.0	
8. Complete fertilizer—K <sub>2</sub> SO <sub>4</sub> .....	10.0	9.5
9. Complete fertilizer—NaNO <sub>3</sub> .....	8.2	
10. Complete fertilizer—NaNO <sub>3</sub> .....	8.5	8.3
11. Complete fertilizer—CaCO <sub>3</sub> .....	10.0	
12. Complete fertilizer—CaCO <sub>3</sub> .....	8.0	9.0

An experiment testing the effect of various fertilizers upon the growth and development of digitalis in soil was determined. Ordinary 5-inch flower pots were filled with 1,000 Gm. of a clay loam soil, taken from the premises of the Mulford Biological Labora-

<sup>3</sup> Complete fertilizer—1,000 lbs. CaCO<sub>3</sub>, 800 lbs. Ca(H<sub>2</sub>PO<sub>4</sub>)<sub>2</sub>·2H<sub>2</sub>O, 400 lbs. K<sub>2</sub>SO<sub>4</sub>, 600 lbs. NaNO<sub>3</sub> and 100 lbs. MgSO<sub>4</sub> per acre of 2,000,000 lbs.

tories. Fertilizers were applied as shown in the table below. Seeds were planted on May 28, and about 6 months later, the plants were harvested and dried in the oven at 100° C. for 4 days. The moisture conditions were maintained at the physical optimum of the soil.

On studying the results of Table II, it will be seen that adding fertilizers to this heavy clay loam soil increased the growth of digitalis to some extent, however, in most of the cases, the increase was comparatively small. In the determination where a complete fertilizer was applied, the increase in weight over the control was greatest. In the pots where no sodium nitrate was added, the weights of digitalis harvested was very little more than in the control which received no fertilizer.

To more fully determine the absolute fertilizer requirements of digitalis plants, the above recorded fertilizer experiment was repeated using sand. The results of this experiment are presented in Table III.

TABLE III.  
 SHOWING THE EFFECT OF INORGANIC FERTILIZERS UPON DIGITALIS PLANTS IN SAND.

Lab. No.	Fertilizer Application.	Weight of Plants, Grs.	Average, Grs.
421	No fertilizer .....	1.7	1.4
422	" " .....	1.3	
423	" " .....	1.1	
424	Complete fertilizer <sup>4</sup> .....	4.7	3.1
425	" " .....	2.3	
426	" " .....	2.4	
427	Complete fertilizer—Ca(H <sub>2</sub> PO <sub>4</sub> ) <sub>2</sub> ·2H <sub>2</sub> O.	1.5	1.5
428	" " " .....	1.9	
429	" " " .....	1.2	
430	Complete fertilizer—K <sub>2</sub> SO <sub>4</sub> .....	3.9	3.7
431	" " " .....	3.7	
432	" " " .....	3.5	
433	Complete fertilizer—NaNO <sub>3</sub> .....	2.2	2.3
434	" " " .....	2.5	
435	" " " .....	2.3	
436	Complete fertilizer—CaCO <sub>3</sub> .....	3.5	3.2
437	" " " .....	2.3	
438	" " " .....	3.8	

It is very apparent from the results shown in Table III that certain inorganic fertilizers were necessary for the maximum growth

<sup>4</sup> Complete fertilizer—I,000 lbs. CaCO<sub>3</sub>, 800 lbs. Ca(H<sub>2</sub>PO<sub>4</sub>)<sub>2</sub>·2H<sub>2</sub>O, 400 lbs. K<sub>2</sub>SO<sub>4</sub>, 600 lbs NaNO<sub>3</sub> and 100 lbs. MgSO<sub>4</sub> per acre of 2,000,000 lbs.



of digitalis. Phosphorus and nitrogen seemed to be the elements which the digitalis plants needed most. In the determinations where no phosphorus was supplied, the growth of digitalis was about the same as the controls. This would indicate that the other fertilizers supplied were not effective in increasing the plant growth until some available phosphorus was furnished. There seemed to be sufficient potash and lime in this sand to fulfill the needs of digitalis, as the growth of digitalis in the determinations where these were absent: 430, 431, 432 and 436, 437, 438, respectively, was as large as that in the determination receiving a complete fertilizer.

#### EFFECT OF CERTAIN INORGANIC SALTS UPON THE GROWTH AND ALKALOID CONTENT OF DIGITALIS.

Certain inorganic salts stimulate the growth of some agricultural plants. Salts of manganese have this property. Boname (4) and others have shown that manganese in small amounts occurs in various soils and plants. Rogers and Newcomb (13) state that manganese appears to be a constant constituent of digitalis leaves, but the amount varies with the source from which the samples are obtained. Alpers (2) states that digitalis is generally found growing in soil which contains iron and manganese. It is true that all soils contain a certain amount of iron and according to Boname (4), soils contain a certain amount of  $MnO_2$ . According to Gehe (2), it is due to the lack of these elements (Mn and Fe) that digitalis does not occur in Switzerland.

To determine if salts of manganese or iron affected either the growth or the alkaloid content of digitalis when grown in soil, a pot experiment was carried out under controlled conditions. Into each of fifteen 5 inch pots, 1,000 Gm. of a clay loam soil (the same as used in the above pot experiment) were weighed. The same amount of a complete fertilizer of 800 lbs.  $Ca(H_2PO_4)_2 \cdot 2H_2O$ , 400 lbs.  $K_2SO_4$ , 600 lbs.  $NaNO_3$ , 1,000 lbs.  $CaCO_3$  and 100 lbs.  $MgSO_4$  per acre of 2,000,000 lbs., was added to each pot. To six pots, manganese sulphate ( $MnSO_4 \cdot 5H_2O$ ) in amounts usually applied in field experiments with agricultural crops, was added; to six others, ferrous sulphate ( $FeSO_4 \cdot 3H_2O$ ), and the other three determinations were used as controls receiving neither salts of Mn or Fe. Digitalis seed was planted in these pots on May 28, and after the plants were about 2 inches high, they were thinned out to an equal number in

each pot and harvested after six months. The moisture was maintained at the physical optimum of the soil. After harvesting, the digitalis leaves were dried and the alkaloid determinations made.

TABLE IV.

SHOWING THE EFFECT OF MANGANESE SULPHATE AND FERROUS SULPHATE, APPLIED TO A CLAY LOAM SOIL, UPON THE GROWTH AND ACTIVITY OF DIGITALIS.

Pot No.	Treatment Lbs. per Acre of 2,000,000 Lbs.	Weight of Dry Material in Gms.	Average Weight in Gms.	Activity, Per Cent.
701	No treatment . . . . .	6.5		
702	" " . . . . .	5.0	6.1	83
703	" " . . . . .	6.7		
704	75 lbs. $\text{MnSO}_4\cdot 5\text{H}_2\text{O}$ . . . . .	7.0		
705	" " " . . . . .	8.0	7.0	76
706	" " " . . . . .	5.9		
707	150 " " . . . . .	7.2		
708	" " " . . . . .	6.5	6.6	100
709	" " " . . . . .	6.2		
710	75 " $\text{FeSO}_4\cdot 3\text{H}_2\text{O}$ . . . . .	7.7		
711	" " " . . . . .	6.2	6.5	90
712	" " " . . . . .	5.7		
713	150 " " . . . . .	6.5		
714	" " " . . . . .	6.0	6.1	90
715	" " " . . . . .			

The results of the experiment above show that neither application of manganese or iron sulphate were effective in increasing the yield of digitalis in this soil, as the results are all within experimental error. From this, we would conclude that this soil either was sufficiently supplied with manganese and iron for the needs of digitalis, that the absorptive and adsorptive effects of this soil were so great that such amounts as were supplied were taken from the field of activity when they could be utilized by the plant, or that these salts were not essential for digitalis. There was a considerable variation in the activity of the samples of digitalis harvested from the pots which received the various treatments of the salts. This difference in activity is most marked between the samples receiving no treatment and those using 150 lbs.  $\text{MnSO}_4\cdot 5\text{H}_2\text{O}$ . Applying this amount of  $\text{MnSO}_4\cdot 5\text{H}_2\text{O}$  was effective in increasing the activity 17 per cent. over that of the control. In the case of the determination receiving iron, there is an indication of increase in activity but this may be almost within experimental error.

## INSECTS AND DISEASES AFFECTING DIGITALIS.

Digitalis plants, quite different from hyoscyamus and belladonna, Koch (8), (9), are not attacked by the various chewing and sucking insects. Hence, they require no spraying nor such particular attention as hyoscyamus and belladonna. It was noted that grasshoppers will chew the leaves, but as yet, the destruction by grasshoppers has been negligible.

A fungus disease, having all the characteristics of root rot, was found present on several digitalis plants in the field. This did not prove very destructive, as only a few plants were attacked and in these cases, the plants withstood the attack of this fungus.

EFFECT OF DRYING AT DIFFERENT TEMPERATURES UPON THE  
ACTIVITY OF DIGITALIS.

Opinions with regard to the methods of drying digitalis leaves, seem to differ considerably. Alpers (1) says the leaves should be dried at once as completely as possible, in a well ventilated drying closet at a temperature not exceeding 100° C. Perrot and Goris (3) propose the method of sterilizing the leaves, thus destroying the enzymes, when first drying digitalis leaves.

Borneman (5) concludes that the digitalis plants should be dried quickly by artificial heat, the temperature being brought up to 100° C. as soon as possible and maintained at this point.

Newcomb (12) summarizes in drying digitalis, applying artificial heat in a closet at a temperature of 75 to 100° C. for 8-10 hours a day, required 3 days to reduce the moisture to 4 per cent. By this method, the green color was never lost. He says that these methods were particularly suitable in that the leaves were quickly dried, it fixed the desirable green color, and at the same time, the active principles were not in any way injured.

An experiment on determining the effect of drying under various conditions on the activity of digitalis leaves, was made. A large sample of about 6 kilos of digitalis leaves was cut into small portions. After thoroughly mixing this material, it was divided into five samples of equal size. Each of these samples were dried at a different temperature, as shown in the table below. After drying these samples, they were submitted for analysis.



TABLE V.

SHOWING THE ACTIVITY OF DIGITALIS LEAVES DRIED AT VARIOUS TEMPERATURES.

Sample No.	Conditions of Drying.	Activity Per Cent.
1.	Out of door temperature 28° C. ....	166
2.	In oven 55-60° C. ....	142
3.	In oven 100° C. ....	166
4.	Heated in oven at 100° C. 1 hr. then dried at 55-60° C. ....	166
5.	Heated in autoclave 15 lbs. pressure for 1 hr. then dried at 55-60° C. ....	125

That the conditions of temperature under which digitalis leaves are dried influence their activity is quite apparent. The samples dried in the oven at 100° C., and heated in the oven at 100° C. for an hour then dried at 55-60° C. had the same activity as that which was dried spontaneously at a temperature of 28° C. On comparing the results of the three above mentioned with the results of the sample dried at 55-60° C., it is seen that 55-60° C. is an undesirable temperature, if the highest activity is to be secured. The explanation for the low results of the sample dried at 55-60° C. as compared with that dried at 100° C., is that in the former case, the activity might have been lost due to enzyme action as has been stated by investigators, previously referred to, while in the latter case, the enzyme activity was stopped at once. Autoclaving at 15 pounds pressure for one hour then drying at 55 to 60° C. proved too destructive, as the results of samples treated by this method were 41 per cent. less in activity than the sample which was heated in the oven at 100° C. and then dried at 55 to 60° C.

## SUMMARY.

From the results of the experiments with digitalis, we summarize as follows:

1. The ordinary blotting paper method proved satisfactory for determining the viability of digitalis seeds.
2. By the blotting paper method, using good viable seed, 86 per cent. germinated in 9 days.
3. The viability of digitalis seed was variable, being from 7.5 to 91 per cent. viable.
4. When planting digitalis seeds in soil, most of the seeds had sprouted and were  $\frac{3}{4}$  of an inch high on the 6th day after planting.
5. The most economical method of securing digitalis plants in the greenhouse, is to sow the seed directly in small pots. After

they have reached the height of 2 inches, thinning them out to from 3 to 5 plants per pot and then letting them grow several weeks longer before planting in the field.

6. From the practical standpoint, seeding digitalis directly in the field proved unsuccessful.

7. Inorganic fertilizers applied to a clay loam soil were effective in increasing the yield of digitalis. A complete fertilizer of 1,000 lbs.  $\text{CaCO}_3$ , 800 lbs.  $\text{Ca}(\text{H}_2\text{PO}_4)_2 \cdot 2\text{H}_2\text{O}$ , 400 lbs.  $\text{K}_2\text{SO}_4$ , 600 lbs.  $\text{NaNO}_3$  and 100 lbs.  $\text{MgSO}_4$  per acre of 2,000,000 lbs., gave the best results. With this soil, sodium nitrate seemed to be the most essential single fertilizer.

8. In sand, calcium phosphate (monobasic) was the most important single fertilizer necessary for digitalis.

9. Neither manganese sulphate nor ferrous sulphate, applied in amounts of 75 or 150 lbs. per acre of 2,000,000 lbs. of a clay loam soil, encouraged a larger growth of digitalis. One hundred and fifty pounds per acre of manganese sulphate applied to a clay loam soil, increased the activity of digitalis 17 per cent. over the activity produced in plants grown in soil receiving no manganese sulphate.

10. Chewing or sucking insects do not seem to attack digitalis plants. A fungus disease, which has all the characteristics of a root rot, attacks digitalis plants, but has not been found to be very destructive.

11. Drying digitalis leaves at  $100^\circ \text{C}$ ., or heating for one hour at  $100^\circ \text{C}$ . and then drying at  $55\text{--}60^\circ \text{C}$ ., were the most satisfactory methods from the standpoint of both the amount of activity, as well as from the speed with which the drying is accomplished.

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## THE PHARMACEUTICAL CHEMIST AND THE SCOPE OF HIS WORK.<sup>1</sup>

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Each of us is prone to magnify the importance of that particular branch of chemistry in which he is actively engaged, so perhaps I may be pardoned for what, to many of you, may seem a biased and erroneous opinion, or evidence of a dense ignorance concerning other fields of chemical endeavor, when I say that I believe no field of chemistry is of greater scope or more varied character than that of pharmaceutical chemistry. And yet, I hope to give you such reasons for the faith that is in me that, if not fully agreeing, you

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may at least recognize a measure of justice in this claim and have a better understanding of the reasons back of it.

Pharmacy has to do with the compounding and dispensing of medicinal products and is most frequently thought of in the very narrow sense of mere mixing together of various individual substances, or the extraction of drugs with the proper solvents and dispensing in suitable form for use, the whole process involving only a very moderate degree of chemical knowledge.

It is to this extremely limited scope that the term "pharmaceutical chemistry" is all too frequently confined. I wish to direct your attention, however, to pharmaceutical chemistry in its broadest sense as being the chemistry of medicinal substances, pertaining to their origin, preparation, dispensing, and effects, and the remarkable and varied ramifications of these subdivisions. Far from being a limited and somewhat isolated division of chemical science there is, I believe, no other branch of chemistry that needs for the solution of its diverse problems so many otherwise distantly related portions of chemical knowledge.

The metallurgist, who from the iron ore of northern Michigan produces by reactions in blast furnace and Bessemer converter, iron and steel of varied composition; or from the scarlet cinnabar of southern California wins the mercury for use in physical instruments and amalgams; or from the ores of Missouri obtains in giant smelters the zinc for innumerable industrial uses, may often forget that iron is intimately associated with vital processes, as in the red blood corpuscles, and plays an important rôle as a curative agent; that the mercury salts are used in combating some of the most deadly and insidious diseases, or as highly effective germicides and antiseptics; that the zinc in one form may be intensely escharotic and in another may be the basis of mild and healing ointments of wide use.

The agricultural chemist, who makes two blades of grass or ears of wheat grow where only one grew before, may also develop digitalis or belladonna or hydrastis or cannabis in greater abundance or of higher potency.

The glass chemist may have his skill taxed to produce ampoules of glass free from excess alkali and easily workable in a blow-pipe flame or free from soluble iron salts that rapidly decompose such substances as hydrogen peroxide or adrenalin.

The coal-tar industry contributes from its cruder products the

so-called "dead oils" as a basis for disinfectants of considerable potency; pure cresylic acids, to make antiseptics for surgical or general use; and phenol for use as such or in various compounds such as phenyl salicylate (salol) or the phenolsulphonates of zinc and calcium.

The dye chemist furnishes for medicinal use such things as phenolphthalein, so widely employed as a laxative; phenolsulphonaphthalein as a test for activity of the kidneys; scarlet-red for stimulating healthy and rapid growth of skin over surfaces denuded by burns or other accidents; acriflavine, but recently recommended in solution as a surgical dressing for extensive wounds, to be used in a manner similar to the sodium hypochlorite solution, known as Dakin's Solution, being destructive to bacteria in high dilution and apparently harmless to living tissues; malachite green proposed and widely experimented with for the same purposes; or methylene blue, so extensively used in certain types of urethritis.

Physical chemistry lends its aid in the production of such remedial agents as colloidal solutions of silver, mercury, sulphur, etc., obtained either by direct electrolytic action or in the presence of proteins, and adds to our slowly acquired empirical knowledge of emulsions an understanding of the reasons why, and the conditions under which the best results may be obtained.

Radiochemistry finds its pharmaceutical application in the use of ultra-violet rays for sterilizing water or various solutions, or the employment of radium salts and radioactive solutions in the treatment of various diseases, notably cancer.

The petroleum industry gives to the pharmaceutical chemist solid and liquid petrolatum of varying degrees of purity ranging from cruder petrolatum for veterinary ointments to the most highly purified liquid oil intended for human use as an intestinal lubricant, and paraffin as an ingredient of ointments or base of surgical dressings for application to extensive superficial wounds or burns.

The consideration of oils and fats, both vegetable and animal, applied one way or another to medicinal use, opens up another wide range through which our chemical investigations may lead us, including such things as the familiar castor and cod-liver oils; the intensely active cathartic, croton oil; that relic of old-time pharmacy, citrine ointment, made from lard, nitric acid, and mercury by a process similar to the familiar elaidin test for olive oil; the comparatively little known chaulmoogra oil, which has been used with

some measure of success in the treatment of leprosy in India and our own southern states, and was some years ago the subject of extensive chemical investigation; oil of chenopodium or American wormseed, used first as an ordinary anthelmintic and more recently as a highly successful agent in destroying the hookworm, the bane of existence to so many thousands of people in warmer climates; and a great array of other fixed and volatile oils. And these things suggest at once a multitude of gums and resins of more or less interest medicinally, but which we will pass by.

In that limitless domain to which we refer in general as "organic chemistry," including therein those things particularly connected with physiological and biological chemistry, there exists a tremendous number of substances of great interest to the pharmaceutical chemist and there lie before him untouched fields for investigation that almost stagger the imagination. In this category appear substances of natural origin and of synthetic production—the alkaloids of aconite, opium, belladonna, stramonium, ergot, nux vomica; the comparatively innocuous glucosides of cascara or the highly toxic ones from strophanthus and digitalis; the digestive ferments such as pepsin, diastase, pancreatin; the endocrine glands and their derivatives, such as the suprarenal whence comes adrenalin, so marvelously potent in its effects on the blood pressure that one-twentieth of a milligram will show pronounced effects on a man; the thyroid, from which but recently an active iodine-bearing substance has been isolated; the pituitary gland of inestimable value in obstetrical practice and in the treatment of surgical shock; and others still less understood. Then we have that formidable and continually increasing array of synthetic substances, some of which, like acetylsalicylic acid (aspirin), or acetphenetidin (phanacetin), are part of the equipment of almost every household medicine cabinet, and others that you and I never heard of and probably never will.

These brief citations give some idea of the infinite variety of work presented to the chemist who deals with medicinal products but do not give any adequate conception of the great number of unsolved and abstruse problems which still lie before us and to which I will refer presently. You can at least see that the chemical knowledge of the man who has to do with pharmaceutical problems in their fullness must be extensive and that he will certainly have no monotonous existence.



Specific examples of some of the interesting questions that arise, which in some instances are very easy of solution and in other cases give us problems that promise to remain unsolved for an indefinite time in the future, will serve to give a more concrete conception of the requirements of the man who has to do with the development and production of medicinal substances in their widest scope.

Remember also that sometimes the solution of the simplest problems may involve the saving of hundreds or even thousands of dollars to the manufacturer who is producing medicinal substances on a very large scale. A question that may be of no particular moment when the quantity involved is only a few ounces becomes of intensest interest when it may mean the difference between entire loss or the satisfactory distribution of hundreds of pounds or thousands of pints of medicinal compounds of properly high quality.

Take so simple a thing as the almost universally used mild tonic, Beef, Iron, and Wine. Why should continual trouble be experienced with the development of pressure in the bottles, the evolution apparently of carbon dioxide, and continual breaking of packages and consequent loss? "Fermentation, of course," will be your first answer, and the fact that carbon dioxide is evolved seems excellent evidence that this supposition is correct, but fermentation is not likely to occur in a product that contains 18 per cent. alcohol, and furthermore, this explanation is impossible when the trouble continues after the product has been thoroughly sterilized in an autoclave and proven sterile by bacteriological tests. The solution when found is very simple and is that due to the action of the actinic rays of light the ferric citrate in the slightly acid solution is reduced to a ferrous salt with liberation of carbon dioxide. If a ferrous salt is originally used, there is no such trouble, and if the ferric salt is employed, the product must be carefully protected from bright light, especially direct sunlight.

Take another case: Why should breakage in ampoules containing cacodylates be very much greater than with any other of the solutions usually prepared in this form? There was no pressure developed and no decomposition of the solutions could be detected. The fact that the breakage occurred largely at the extreme end of the capillary tip, where the ampoule is finally sealed in a blowpipe flame, gave a clue, and the solution of the problem was that traces of the cacodylate solution adhering to the glass were decomposed just at the tip where the flame is used for sealing; the arsenic com-

bined with the glass, forming a ring of arsenical glass, which is entirely different in coefficient of expansion from the remainder of the ampoule and very brittle, hence comparatively slight changes in temperature frequently caused the tip to snap off. On putting into effect means for carefully washing out the tip of the ampoule with distilled water before sealing, the trouble disappeared.

Again, in the manufacture of antiseptic tablets containing corrosive sublimate, some suitable diluent is used that will be completely soluble in water and if possible aid in the solution of the mercuric chloride without reacting with it chemically; for this purpose ammonium chloride or citric acid is commonly used. In some few instances both together have been employed. To prevent the material sticking to the dies on a tablet machine, some lubricant is necessary, and as a comparatively soluble substance, antiseptic in itself, boric acid is often employed in a case of this kind. A quantity of tablets began to evolve considerable amounts of hydrochloric acid gas, sufficient to rapidly attack tinned-iron containers shortly after they were made. It was found that the boric acid used as a lubricant, in the presence of citric acid, reacted upon the ammonium chloride with the evolution of hydrochloric acid. The omission of either the boric or citric acid immediately remedied the trouble.

Another problem that seemed on the face of it so simple that it was really no problem at all was the obtaining of material such as sodium chloride, milk sugar, and alkaloidal salts of such purity that they would give a solution in distilled water *completely free* from insoluble floating particles. I would not go so far as to say that it cannot be done; I think that conditions are conceivable under which it might be accomplished; but I have never seen it done, and upon a commercial scale it has, so far as I know, never been accomplished. You must remember, of course, that the floating particles thus referred to are minute, though easily visible to the naked eye. Some years ago it was desired to prepare C.P. sodium chloride in crystalline form suitable for redissolving in distilled water for intravenous injection. No sodium chloride of sufficient purity was obtainable on the market, and in attempting to make a quantity, it was found that during evaporation in a carefully purified solution, the sodium chloride would attack tinned copper, aluminum, and several grades of special enameled iron to such an extent that the crystals when redissolved in water would show a weighable

amount of insoluble matter. The best thing available was one particular grade of resistant enamel, though had it been available on a commercial scale, a pure silver pan would probably have been just as effective.

When it comes to milk sugar or alkaloidal salts, it would seem that all that is necessary is to carefully filter the solution and evaporate, to obtain a product that will redissolve in distilled water without showing any signs of floating particles. When you come, however, to critically examining such solutions, you will discover that the first thing is to get distilled water which under the most rigid tests will show no tiny particles floating in it. So far I have never seen any of the above mentioned substances or distilled water that would show absolutely no signs of tiny floating particles when viewed by the naked eye against a dark background under an electric light. Remember, though, that one liter or even five liters of such a solution will leave no weighable residue on a filter paper; in fact, unless the filter is hard and smooth it is very likely to make the solution worse.

After problems connected with the manufacture are solved, there come up also numerous questions in regard to containers used. For example, glass that contains any trace of alkali soluble in water (and this is the rule rather than the exception) cannot be used in making ampoules containing very delicate substances, for strychnine alkaloid will be precipitated from its salts and a delicate organic preparation like adrenalin will be quite rapidly destroyed. Containers made from coke tin plate cannot be used to hold materials that might slowly attack iron, whereas charcoal tin plate is satisfactory, the difference being that the former has occasional exceedingly minute holes through the tin, while in the latter the tin coating is uniform and unbroken.

When we come to the consideration of the more difficult problems connected with medicinal substances and their development we reach a vast unknown region that has been but most imperfectly explored. We speak glibly oftentimes of relationship between chemical constitution and physiological action, but our actual and definite knowledge of the relationship is at the best extremely limited. We have acquired what seems like a considerable amount of empirical understanding that certain effects are in some way associated with certain combinations of elements or radicals, but we may draw a hasty conclusion merely to find that there are numerous exceptions



to our supposed "law." For example, pyrocatechol (ortho-dihydroxy-benzene) is more poisonous than its monomethyl derivative, guaiacol, which in turn is more potent than the dimethyl derivative, veratrol. Apparently we are on the road to prove that alkylation of a hydroxy group in aromatic compounds decreases the toxicity, but presently we find that from resorcinol, which is meta-dihydroxy-benzene, we obtain a dimethyl derivative that is very much more toxic than the parent substance and our interesting theory suffers a rude shock.

If now we cautiously advance along some of the blazed trails in the jungle of organic compounds, hoping fervently that harsh and unrelenting facts will not pounce upon and tear to pieces some of our nicely domesticated pet theories, we discover some rather astonishing things. Take adrenalin, which, as derived from its natural source, is levorotatory. When prepared synthetically it is racemic and much less active than the naturally occurring form. Further investigation shows that the dextrorotatory form is only about one-twelfth as powerful in increasing the blood pressure as the levorotatory form. The peculiar effect of the atropine group of alkaloids in dilating the pupil of the eyes is about fifteen times as great in levohyoscyamine as in its stereoisomer. Atropine and cocaine are not widely different chemically, both being derivatives of the nucleus tropine, but while some points of likeness may be found in their physiological action, there are many and pronounced differences, for instance, cocaine is a powerful local anesthetic, while atropine is devoid of this effect. Again, cocaine is methyl-benzoyl-ecgonine and ecgonine has no local anesthetic properties, while neither benzoyl-ecgonine nor ecgonine-methyl ester have more than a very slight effect of this kind. And so we go, gradually accumulating a great store of isolated facts and laboriously fitting them together. We are very like the child with a jig-saw picture puzzle: we fit together a few facts here and a few more over there and occasionally have to take apart some which do not fit perfectly, hoping that some day we will get enough of this picture together to find out what it really looks like.

Turning for a moment to other questions, how shall we determine the medicinal activity of aconite preparations? The drug contains one important and highly toxic alkaloid, aconitine, but also varying amounts of related alkaloids which are not only much less toxic but in some cases actually antagonistic in their action to the aconi-

tine. The aconitine itself is very easily affected by heat, especially in the presence of moisture, and decomposes into various other bodies which possess quite different physiological action. One can obtain concordant results on repeated chemical assays, and find that they fail entirely to agree with the physiological activity as determined by tests on animals. Both the physiological tests and the chemical assay seem to be affected by the presence of secondary alkaloids. The present situation as regards the determination of the activity of aconitine preparations is in a very unsatisfactory state.

For over 100 years we have known that the most important alkaloid of opium is morphine, but only within the past 10 years have we come to a definite understanding of its chemical constitution, and though at present morphine is worth \$200 per pound, there is no commercially available process for producing it synthetically.

Then there is that class of substances known as enzymes, typified among medicinal agents by pepsin, pancreatin, and diastase. We have for years used these products, particularly pepsin, as an aid to imperfect digestive activity, but do not yet know their exact constitution. Most extensive investigations have been pursued regarding the nature of pepsin, and it has been possible to produce a material under this name of such strength that one part will digest 50,000 parts of coagulated egg albumin, showing a tremendous power of protein digestion. Even here apparently the limit is not reached, and we have not succeeded in isolating any definite substance whose chemical identity we can establish.

Pancreatin is known to be a mixture of several different enzymes, but we are no better acquainted with the constitution of any of them than we are with that of pepsin. Besides these substances there are numerous other enzymes of more or less importance that occur either in vegetable or animal life, and many of which undoubtedly have important rôles to play in connection with vital processes, and as we come to understand them better we may find some of them of great service in dealing with diseases that are now but imperfectly understood.

In investigating enzymes we are struck with the similarity in many respects between catalytic action of these organic substances and those inorganic colloidal solutions of metals that are quite extensively advocated as remedial agents. For instance, both are rendered inactive by boiling and are affected by the reaction of the

medium in which they act. The decomposition of hydrogen peroxide by catalase, which reaction may be used for the quantitative determination of this enzyme in the blood or liver, or the similar decomposition by colloidal solution of platinum, both proceed more rapidly in a slightly alkaline medium. The presence of a trace of hydrocyanic acid acts as a distinct poison, and inhibits the activity both of enzymes and colloidal solutions, though there are some exceptions to this rule. What is the chemical reason back of these resemblances between substances that seem otherwise so dissimilar?

One of the scourges of humanity in Eastern Asia, the Philippines, Borneo, Sumatra, and the Straits Settlement has been a disease known as *beri-beri*. This through long and laborious investigations was found to be connected with the type of food used, being especially prevalent where polished rice was the main article of diet. It was found that a very remarkable and rapid improvement in the condition of those afflicted with this disease could be produced by extracts from the husks and polishings removed from rice. Continued investigation has led to recognition of certain bodies called "*vitamines*" present not only in the pericarp of rice but also in other grains, in yeast, and in a number of different plants. The name has been given because it is known that these substances are related to the amines and are so intimately associated with vital processes. They are present in only exceedingly minute amounts and yet their effect is very great. To the presence or absence of the same compounds has been traced the disease quite prevalent in our own southern states, known as "*pellagra*."

We are just beginning to understand that these *vitamines*, which all these years we have taken into our systems with our daily food, have in some way a tremendous effect upon our health, but how widely they are distributed or what their chemical constitution is and how they may differ as derived from different sources, and why they are so necessary to our healthful existence, still remains almost a complete mystery. Few, if any, greater fields for chemical investigation of medicinal substances exist at present than that of the *vitamines*.

Some 400 years ago Paracelsus founded what came to be known as the School of Iatrochemistry, on the assumption that the human body was made up of chemical substances and that illness was caused by chemical changes in the organs and juices of the body, and that to cure these ills chemical compounds must be found that



would restore the original healthy condition. This fundamental principle was so obscured by fantastic ideas and was carried to such extremes by overzealous followers that it fell into disrepute and finally disappeared entirely, giving place to a chemistry founded on careful experimentation rather than fanciful theories. Strangely enough we are now returning, but under very different auspices, the limitations of our knowledge and the fact that we must not be too eager to draw conclusions from the isolated facts we know, but as in former days the practice of pharmacy and the art of healing did much to develop chemical knowledge, so to-day must chemistry in its fullest application go far toward improving our means of treatment and control over disease.

PARKE, DAVIS AND COMPANY,  
 DETROIT, MICH.

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## THE TRADE IN CINCHONA BARK.<sup>1</sup>

BY B. F. HOWARD.

An article on "The Future of the Trade in Cinchona Bark" appearing in the last issue of the *Bulletin of the Imperial Inst.*<sup>2</sup> contains much information of value to those who desire to have an authoritative résumé of this important subject.

An interesting introduction traces briefly the history of the natural Cinchonaceæ of the forests of the Andes, and the botanical classification of the varieties best known on the market at the present day. Turning to the production of cultivated bark, the author gives the output in recent years from the plantations in the Dutch East Indies, India and Ceylon, and shows clearly the enormously important part played by the Dutch plantations in Java. In recent years, Java heads the list of producers with an annual output of 22,880,000 lbs., India supplying 2,000,000 and other countries 440,000 lbs. Perhaps these figures should be taken as a general indication of the pre-eminence of Java rather than as an exact comparison, for whereas the Java production is based on an average of the years 1911-1913, the Indian output given is the average of the years 1912-1913 to 1915-1916, and this must surely have been affected by the difficulties of production and shipping during the war.

<sup>1</sup> Reprinted from *Jour. Soc. of Chem. Industry*, February, 1919.

<sup>2</sup> XVI, Pt. 3, 1918.

The commercial or market aspect is then briefly dealt with and the efforts—successful in the main—described which were adopted to prevent over-production in the years before the war. Under a heading entitled “Trade in Cinchona Bark and Quinine,” the author shows that although the Indian plantations and factories are unable to supply the needs of that portion of the Empire, yet the bulk of the imports of manufactured quinine into India have hitherto been from British sources.

A series of import and export tables follows showing the high percentage of the quinine requirements of the United Kingdom which was formerly supplied by Germany—a typical example of the position of the fine chemical industry in this country before the war, and a state of affairs which, we trust, has now gone for ever.

The great importance of local manufacture of quinine salts in Java and its possible future bearing on the world's quinine trade is not mentioned, probably owing to the complexity of the problem and the difficulty of obtaining accurate information. It is obvious, however, that no account of the cinchona industry which ignores this important factor can be considered complete.

The final portion of the article deals with bark produced in St. Helena and East Africa. Although from a commercial point of view these plantations are at the moment negligible, yet from the scientific aspect the typical analyses given are of considerable interest as they show a high percentage of quinine and prove the bark to be well up to the Java standard, thus indicating most successful cultivation—which may have been either deliberate or accidental. Viewed in detail the tables giving the results of examination of these barks appear to be somewhat inadequate and to lack uniformity. Although the total alkaloid figure and the percentage of quinine sulphate are given, a complete separation of the four principal alkaloids has apparently not been attempted. Again, the results are complicated by the inclusion of the percentage of moisture found, but as bark is valued on its alkaloid contents as shipped, moisture is not a factor of any importance. A more practical method of stating the results would be to give the percentage of (hydrated) sulphate of each of the alkaloids (quinine, cinchonidine, quinidine and cinchonine), together with the percentage equivalent of alkaloid in each case; also the sum of these figures and the amount of amorphous alkaloid. So tabulated, the results of the analyses of these very interesting samples would have enabled the

reader to evaluate the barks commercially, as well as to derive useful additional scientific information from them.

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[Contribution from the Research Laboratory and the Department of Glandular Extracts, Parke, Davis & Co.]

## STUDIES ON PEPSIN. I. CHEMICAL CHANGES IN THE PURIFICATION OF PEPSIN.<sup>1</sup>

BY LEWIS DAVIS AND HARVEY M. MERKER.

The question of the chemical composition of pepsin has occupied the attention of a number of investigators. Following the classical researches of Pawlow<sup>2</sup> and his pupils, Pekelharing<sup>3</sup> appears to have been the first to undertake purification of the enzyme. This investigator prepared a light yellow powder which, while readily soluble in dilute acids and sodium chloride solution, dissolved with difficulty in water but showed strong peptic activity. It gave reactions for albumin, but was believed to contain a soluble phosphorus compound as an impurity. On boiling pepsin solutions, Pekelharing obtained a nucleoproteid and was able, under certain conditions, to separate an albumose.

Nencki and Sieber,<sup>4</sup> using as initial material juice obtained through gastric fistula in dogs, claim to have secured an active pepsin preparation through precipitation which is free from albumin. At the same time, they consider the precipitate of transparent granules containing chlorine which they obtained by strongly cooling the gastric juice to be a chemical individual, and, in all probability, the true enzyme. They also submit analyses to support their contentions. Pekelharing,<sup>5</sup> in a later investigation, in which he employed the artificial gastric juices extracted from several hundred hog stomachs by his previous method, and also the juice obtained from gastric fistula in dogs, disproved this view. He found pepsin

<sup>1</sup> Read before the Biological Section of the American Chemical Society at the Cleveland meeting, September 12, 1918. Reprinted from *The Journal of the American Chemical Society*, February, 1919.

<sup>2</sup> Pawlow, *Centr. Physiol.*, 1888; *Ergebnisse Physiol.*, 1902. i. Part I, 246.

<sup>3</sup> Pekelharing, *Z. physiol. Chem.*, vol. 22, 233, 1897.

<sup>4</sup> Nencki and Sieber, *ibid.*, vol. 23, 291, 1901.

<sup>5</sup> Pekelharing, *ibid.*, vol. 35, 8, 1902.



to be free from phosphorus and to contain no nucleoproteid, but the analyses of his preparations showed no constancy in results.

That a protein-free pepsin solution having digestive action is possible, has also been maintained by Schrumpf.<sup>6</sup> The latter prepared a Büchner-pressed extract of hog stomachs, clarified by filtration, and dialyzed against running water. The dialysate thus obtained was precipitated by addition of cholesterin in alcohol-ether solution, filtered, the precipitate redissolved in water, and the suspension finally clarified by a Kitasato candle. The clear filtrate, while giving none of the protein reactions, still showed powerful digestive activity.

The amino acid constituents of pepsin have been investigated by Hugounenq and Morel<sup>7</sup> using an autodigested, hydrochloric extract of hog stomachs. They conclude that an extract of pepsin contains a number of monoamino acids in the free state, probably formed in the autodigestion. Glycocoll, aspartic and glutaminic acids, and also histidin, they found to be absent in the material examined.

It is thus readily apparent that, as true with other enzymes, the chemical nature of pepsin is still an open question. Nearly all of the above investigators have based their conclusions on crude preparations, undoubtedly containing admixed or combined impurities. Seemingly, no attempt has been made to prove, by quantitative measurements of the proteolytic activity, that an actual purification has taken place, where such is mentioned. The present investigation was undertaken by us to determine what changes take place in the purification of pepsin, with the view of possibly throwing some light on the chemical nature of the enzyme.

#### EXPERIMENTAL PROCEDURE.

*Methods.*—As basic material for purification, a composite lot (consisting of a number of different samples) of 1:2,000 commercial pepsin was employed. Sufficient stock of this mixture was reserved to enable the preparation of all of the various strengths of the enzyme given below. The weaker samples (up to 1:18,000) were prepared by fractional precipitation of a 20 per cent. aqueous solution, while the more active strengths were obtained by salting out the former, filtering and dialyzing. In each case, the final

<sup>6</sup> Schrumpf, *Beitr. Holm.*, vol. 6, 396, 1905.

<sup>7</sup> Hugounenq and Morel, *Compt. rend.*, vol. 147, 212, 1908.

purified material was dried to a constant moisture content of about 5 per cent. and scaled. Assays for proteolytic power were then carried through and the samples analyzed chemically.

Determination of the proteolytic strength of the different samples, made in association with our colleagues, L. M. Gerdes and W. L. Seibert, was in accordance with the method given in the ninth revision of the U. S. Pharmacopœia.<sup>8</sup> The assays were checked in each case, and controlled by running through a standard (1:3,000) pepsin under identical conditions.

The chemical examination included analyses of total mineral matter, total nitrogen, total sulphur by the method of Wolf and Osterberg<sup>9</sup> volumetric estimation, in the ash, of phosphoric acid as  $P_2O_5$ ,<sup>10</sup> chlorides as NaCl,<sup>11</sup> calcium as CaO; also, determination of nitrogen existing in coagulable protein, proteoses by zinc sulphate precipitation,<sup>12</sup> peptones by Bigelow and Cook's<sup>13</sup> modification of Sjerner's method, and amino acids according to Van Slyke.<sup>14</sup> In addition, observations were made in a 2 per cent. aqueous solution of optical rotation, and of the hydrogen-ion concentration. The direct reading ionometer described by Bartell<sup>15</sup> was used in the latter, with a Weston Standard Cell, and the chain: Calomel electrode (*N* KCl)—saturated KCl—pepsin solution—Pt. electrode— $H_2$  at 23°. The complete "set up" employed was similar to that used by Davis<sup>16</sup> in a previous investigation of diphtheria toxin.

Supplementing the preceding, qualitative tests were carried out in accordance with the technique employed by one of us, Davis,<sup>17</sup> with peptone samples. Both a straight 2 per cent. aqueous solution and the filtrate, after coagulating the protein, were used, and examination made for: tyrosin (xanthoproteic, Millon's reaction)

<sup>8</sup> "Pharmacopœia of the United States," 1916, p. 312, 9th rev., P. Blakiston's Son & Co.

<sup>9</sup> Wolf and Osterberg, *Biochem. Z.*, vol. 29, 429, 1910.

<sup>10</sup> "Methods of Analysis, A. O. A. C.," U. S. Dept. Agr., Bur. Chem., *Rev. Bull.*, 107, 4, 1912.

<sup>11</sup> "Standard Methods of Water Analysis," *Am. Pub. Health Ass'n*, 1917, p. 4.

<sup>12</sup> Bömer, *Z. anal. Chem.*, vol. 5, 562, 1895.

<sup>13</sup> Bigelow and Cook, *Journal of the American Chemical Society*, vol. 38, 1496, 1906.

<sup>14</sup> Van Slyke, *J. Biol. Chem.*, vol. 16, 121, 1913.

<sup>15</sup> Bartell, *Journal of the American Chemical Society*, vol. 39, 630, 1917.

<sup>16</sup> Davis, *J. Lab. Clin. Med.*, vol. 3, 358, 1918.

<sup>17</sup> Davis, *ibid.*, vol. 3, 75, 1917.

TABLE I.  
ANALYSES.

Proteolytic, strength (U. S. P. IX.)	Total Mineral Matter, %.	Phosphoric Acid as $P_2O_5$ %.	Calcium as $CaO$ , %.	Chlorides as $NaCl$ , %	Total Sulphur, %.	Percentage of Nitrogen in				Optical Rotation $\alpha_D$ at $24^\circ$ .	Reaction $C_H$ + at $23^\circ$ .
						Total, %.	Coagulable Protein, %.	Proteoses, %.	Peptones, %.		
1:2,000	5.37	1.58	0.26	1.19	0.63	12.93	1.15	0.73	7.37	$-2^\circ 58'$	.....
1:5,500	4.31	1.42	0.32	Trace	0.70	12.60	1.41	1.76	4.78	$-2^\circ 0'$	.....
1:6,000	3.34	1.03	0.46	Trace	0.81	13.41	1.43	2.10	4.91	$-2^\circ 6'$	.....
1:10,000	3.31	1.42	0.35	Trace	0.89	13.55	1.63	3.00	3.73	$-2^\circ 24'$	.....
1:12,000	2.31	1.28	0.29	Trace	0.63	12.95	2.33	3.09	3.41	$-2^\circ 10'$	.....
1:18,000	2.84	1.47	0.71	Trace	1.50	13.47	3.16	3.62	2.68	$-2^\circ 30'$	.....
1:21,000	2.38	1.29	0.58	Trace	0.82	12.57	3.69	3.91	3.73	$-2^\circ 0'$	.....
1:24,000	2.84	1.27	0.52	Trace	0.77	12.64	3.98	4.10	0.96	$-2^\circ 4'$	$2.5 \times 10^{-4}$
1:28,000	1.86	1.09	0.53	None	1.62	13.72	4.39	4.32	0.78	$-2^\circ 20'$	$4.0 \times 10^{-5}$
1:40,000	2.01	0.47	1.01	None	1.50	13.77	8.34	4.43	..	$-2^\circ 30'$	$6.0 \times 10^{-7}$



TABLE II.

REACTIONS IN 2 PER CENT. SOLUTION.

Proteolytic Strength. (U. S. P. 1X.)	Character of Solution.	Picric Acid Reaction.	Ammonium Sulphate Reaction.	Millon's Reagent.	Biuret Reaction.	Hopkins-Cole Reagent.	Molisch's Reagent.	Xanthoproteic Reaction.
1 : 2,000	{ Straight { Coag. filtrate	Mod. ppt.	No ppt.	Mod. ppt., reddish Sl. ppt., reddish Heavy ppt., pink	Bluish pink Bluish pink Bluish pink	Ppt., ring No ppt., ring Ppt., ring	Ppt., ring Ppt., ring Ppt., ring	Yellow color ppt., orange Yellow, deep orange Ppt., orange
1 : 5,500	{ Straight { Coag. filtrate	Mod. ppt.	No ppt.	Sl. ppt., reddish Mod. ppt., pink Sl. ppt., pink	Bluish pink Bluish pink Bluish pink	No ppt., ring Ppt., ring No ppt., ring	Ppt., ring Ppt., ring Ppt., ring	No ppt., mod. orange Ppt., mod. orange No ppt., deep orange
1 : 6,000	{ Straight { Coag. filtrate	Mod. ppt.	No ppt.	Heavy ppt., pink Sl. ppt., pink Heavy ppt., pink	Bluish pink Bluish lavender Bluish pink	Ppt., ring No ppt., ring Ppt., ring	Ppt., ring Ppt., ring Ppt., ring	deep orange light orange orange
1 : 10,000	{ Straight { Coag. filtrate	Mod. ppt.	No ppt.	Heavy ppt., pink Sl. ppt., pink Heavy ppt., pink	Bluish pink Bluish lavender Bluish pink	No ppt., ring Ppt., ring No ppt., ring	Ppt., ring Ppt., ring Ppt., ring	orange light orange orange
1 : 12,000	{ Straight { Coag. filtrate	Mod. ppt.	No ppt.	Sl. ppt., pink Heavy ppt., reddish Sl. ppt., pink	Bluish pink Bluish lavender Bluish pink	No ppt., ring Ppt., ring No ppt., ring	Ppt., ring Ppt., ring Ppt., ring	orange light orange orange
1 : 18,000	{ Straight { Coag. filtrate	Mod. ppt.	No ppt.	Heavy ppt., pink Sl. ppt., pink Heavy ppt., pink	Bluish pink Bluish lavender Bluish pink	No ppt., ring Ppt., ring No ppt., ring	Ppt., ring Ppt., ring Ppt., ring	orange red-orange orange
1 : 21,000	{ Straight { Coag. filtrate	Mod. ppt.	Sl. opal	Heavy ppt., pink Sl. ppt., red tinge Heavy ppt., pink	Bluish pink Bluish lavender Bluish pink	No ppt., ring Ppt., ring No ppt., ring	Ppt., ring Ppt., ring Ppt., ring	orange red-orange orange
1 : 24,000	{ Straight { Coag. filtrate	Sl. ppt.	Sl. opal	Sl. ppt., red tinge Heavy ppt., pink Trace ppt., red tinge	Bluish lavender Bluish lavender Bluish lavender	No ppt., ring Ppt., ring No ppt., trace ring	Ppt., ring Ppt., ring Ppt., ring	yellow-orange red-orange faint reddish
1 : 28,000	{ Straight { Coag. filtrate	Sl. ppt.	Sl. opal	Heavy ppt., pink Trace ppt., red tinge Heavy ppt., pink	Bluish lavender Bluish lavender Bluish ppt., lavender	No ppt., ring Ppt., ring No ppt., no ring	Ppt., ring Ppt., ring Ppt., ring	red-orange faint reddish faint reddish
1 : 40,000	{ Straight { Coag. filtrate	Opal	Opal	Opal red tinge	Bluish, no color	No ppt., no ring	Ppt., ring	faint reddish

tryptophane (Adamkiewicz Hopkins-Cole reagent), glycoprotein and glycoproteose (Molisch reagent). Tests were also made on the filtrate from coagulable protein, for proteoses (by addition of saturated zinc sulphate, ammonium sulphate, picric acid solutions), and protoproteoses (by saturated sodium chloride solution, potassium ferrocyanide in acetic acid solution).

*Results.*—Altogether, nine purified products were prepared. Including the basic pepsin material, the various proteolytic strengths of the enzyme which were examined ranged from 1:2,000 to 1:40,000 (U. S. P. IX). The results given in the accompanying Tables I and II, are, in every case, based on duplicate determinations and, because of possible variation in the U. S. P. pepsin assay, these estimations were carried out in triplicate by two different observers.

As may be noted from Table I, the purification of pepsin is accompanied by a general decrease in the total mineral matter. This ranges from an ash content of nearly 5.5 per cent., in the case of the basic (1:2,000) product down to about 2 per cent. with the highest proteolytic strengths obtained. The phosphoric acid content, also, shows a gradual decrease so that the value at 1:40,000 is less than one third that of the basic material. Both the calcium oxide and total sulphur values fluctuate in the different strengths, but both show an increase in the purified as compared with the unpurified samples. It is a significant fact that the chlorides, which are present to the extent of 1.19 per cent. (as NaCl) in the 1:2,000 sample, practically disappear as a result of purification.

Probably the most important data are furnished by the various nitrogen factors, particularly the nitrogen in amino acid condition. Confirming more elaborately the results found by Aldrich,<sup>18</sup> there is found to be almost a uniform decrease in  $\alpha$ -amino acid nitrogen so that in the sample testing 1:40,000 only 0.61 per cent. is found. Corroborating these results, it will be noted from the table that there are steady increases in both the coagulable protein nitrogen and that existing as proteoses, while the peptone nitrogen like that of the amino acids shows a decrease. The values for total nitrogen showed decided variations among the different samples with no significant change as the purification increases.

All of the different strengths of the pepsin examined show levorotation in very nearly the same degree, so that this factor is apparently unaltered as a result of purification. With the exception

<sup>18</sup> Aldrich, *J. Biol. Chem.*, vol. 23, 339, 1915.

of the strongest sample obtained (1:40,000) a slight amount of hydrochloric acid was used in the preparation of the other strengths of the pepsin. As a consequence, 2 per cent. aqueous solutions of these samples show relatively high hydrogen-ion concentration. However, the reaction of the 1:40,000 sample, which is the nearest approach to the pure enzyme, is very nearly neutral ( $C_{H^+} = 6.0 \times 10^{-7}$ ). This would tend to disprove the view held by Jacoby<sup>19</sup> and others that pepsin is an acid.

Consideration of the data presented in Table II shows that the results corroborate, in a general way, the analytical data already discussed. No tests were made on the straight pepsin solutions with saturated picric acid, sodium chloride and ammonium sulphate solutions, and also none with potassium ferrocyanide in acetic acid solution, since the results with all of these reagents, because of coagulable protein would be positive, and practically the same for the different strengths. Confirming the results given in Table I, the saturated picric acid, Hopkins-Cole, and Millon's reagent tests, made of the filtrate after removal of coagulable protein, show presence of amino acid and peptid bodies in the lower strength samples. These gradually disappear so that only traces are found in the highest strength sample of the enzyme. Both saturated sodium chloride solution and potassium ferrocyanide in acetic acid solution gave negative results, indicating absence of protoproteoses in the filtrate from coagulable protein. A positive reaction was obtained in every case with Molisch reagent showing presence of glycoprotein, or its derivatives, in the material. It is significant that the biuret test of the filtrate after coagulation of protein in the 1:40,000 sample, is negative. This would indicate that practically all of the protein material is of the nature of coagulable protein or even more complex in its protein character.

#### DISCUSSION.

A review of the data presented in the foregoing seems to show that in the purification of pepsin there is a gradual elimination of the secondary protein derivatives including amino acids. This is manifested by a constant tendency in the purified samples to approach nearer to the actual character of proteins with increasing proteolytic activity, and is accompanied by an increase in material coagulable by

<sup>19</sup> Jacoby, *Biochem. Z.*, vol. 4, 471, 1907.



heat. From the fact that the highest strength samples still give strong tests with Molisch reagent, it may be possible that the pure enzyme is a conjugated protein, probably a glycoprotein.

Confirming this view, the mineral matter is decidedly less in the purified samples than in the original basic material, approaching almost to the value for pure proteins in the case of the strongest samples. Both sulphur and calcium are probably unaffected by the purification, but there is a decided decrease in the phosphorus content and seemingly a total elimination of chlorides. Other than the increase which would obtain by removal of non-nitrogenous impurities, there is probably not much change in the content of total nitrogen as a result of pepsin purification.

The manner in which the  $\alpha$ -amino acids decrease as the proteolytic activity increases is striking, and seems to be almost proportional in amount. It is noteworthy that the small amount of  $\alpha$ -amino acid present in the sample testing 1:40,000 (0.61 per cent.) very nearly approaches the value for this factor due to lysin as found present by Van Slyke and Birchard<sup>20</sup> in most proteins analyzed by the nitrous acid method.

Results of optical activity determinations are apparently of no significance, since the same values are obtained with several different strengths of pepsin. As already mentioned above, the reaction in aqueous solution of the strongest (1:40,000) pepsin is significant because of its very slight acidity. It would seem very likely, that the concentration of hydrogen ions in solutions of the pure enzyme, when isolated, will probably show only the slight acidity comparable to that given by other proteins.

In connection with the assays of proteolytic strength by the U. S. P. method, it was deemed of interest to make a comparison of the rennetic power of the different samples. It is a significant fact that throughout the entire series, from 1:2,000 to 1:40,000, the rennetic activity and proteolytic strengths are found to go hand in hand. This is being investigated, and will be reported upon in a later paper.

#### CONCLUSIONS.

1. The purification of pepsin seems to consist in the elimination of secondary protein derivatives including  $\alpha$ -amino acids.
2. Calcium and sulphur appear to be unaltered as a result of

<sup>20</sup> Van Slyke and Birchard, *J. Biol. Chem.*, vol. 16, 539, 1914.

purification, but phosphorus is materially reduced. Chlorides are seemingly entirely removed.

3. Aqueous solutions of pepsin, after purification, show no material change in optical activity. A sample of high digestive power (1:40,000), shows a reaction very nearly neutral.

4. Pepsin tends to approach nearer to the actual character of a protein (possibly a glycoprotein) with increasing proteolytic activity.

DETROIT, MICHIGAN.

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## THE ESTIMATION OF PHENACETIN AND OTHER PARA-AMINOPHENOL DERIVATIVES OF HYPOCHLOROUS ACID.<sup>1</sup>

BY A. D. POWELL.

The estimation of the substituted phentidine compounds used in medicine, either alone or in admixture with other substances such as salol and caffeine, has always presented certain difficulties, and various methods have been proposed in recent years for the analysis of mixtures of these substances. Several of these are based on the varying solubilities of the compounds in organic solvents, a more or less complete separation being made, and the separate substances determined gravimetrically. Thus, Seidell<sup>2</sup> proposed a method of this type for the estimation of acetanilide, phenacetin, etc., in "head-ache powders." Emery, Spencer, and Le Febvre,<sup>3</sup> for the estimation of phenacetin and salol, make use of selective hydrolysis, finally reconverting the phenetidine to phenacetin by acetylation, and weighing the phenacetin as such, the salol being estimated by bromine absorption. Another method recently published by Salkover<sup>4</sup> for the separation of these drugs depends on the solubility of salol in petroleum ether, phenacetin and acetanilide being nearly insoluble in this solvent.

Such methods suffer from the obvious defect that they do not sufficiently identify the substances present in the mixture, and the melting-points of the separated constituents cannot always be relied on, owing to the separation not being perfect.

<sup>1</sup> Reprinted from *The Analyst*, January, 1919.

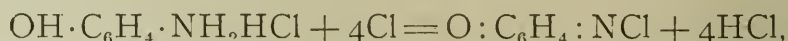
<sup>2</sup> *J. Amer. Chem. Soc.*, 1907, 29, 1088-1091; *The Analyst*, 1907, 32, 360.

<sup>3</sup> *J. Ind. and Eng. Chem.*, 1915, 5, 681-684; *The Analyst*, 1915, 40, 445.

<sup>4</sup> *Amer. J. Pharm.*, 1916, 88, 484-485; *The Analyst*, 1917, 42, 16.

Methods taking into account the chemical constitution of these compounds have also been proposed. Taylor and Vanderkleed,<sup>5</sup> for instance, estimate phenacetin and acetanilide (individually), by steam distillation and titration of the acetic acid produced on hydrolysis. Another method proposed by Emery<sup>6</sup> for the separation and estimation of phenacetin and acetanilide depends on the property of phenacetin of combining with iodine to form an insoluble periodide, acetanilide either not reacting with iodine or producing a soluble compound. The amount of iodine precipitated from solution is determined by titration of the excess left in solution, and the phenacetin content calculated from the figures thus obtained. An iodimetric method for the estimation of phenolic compounds has been published by Wilkie;<sup>7</sup> but this does not appear to have been extended to the aminophenols and phenetidins, although it seems probable that such compounds might form definite iodo-derivatives.

As far as my own experience goes, however, no method has been published in which any characteristic reaction of *p*-phenetidine or *p*-aminophenol has been taken as the basis for the estimation of this group of compounds. The reactions of *p*-aminophenol with oxidising agents were therefore investigated, in order to determine which, if any, could be made the basis of a quantitative estimation. Oxidation by means of potassium dichromate to form quinone was tried, but was found unsatisfactory, as part of the *p*-aminophenol was converted to quinhydrone. The reaction between sodium hypochlorite and an acid solution of *p*-aminophenol was found to be much more promising. These substances react in accordance with the equation:



the quinone chlorimine precipitating as golden-yellow flocks from concentrated solutions, but remaining in solution at dilutions below about 1 per cent.

*P*-phenetidine is also converted to quinone chlorimine by the action of hypochlorous acid. The reaction is quantitative, and provides a rapid means for the estimation of these bases and all their derivatives which yield the free base on hydrolysis.

The direct absorption of chlorine does not form a suitable basis

<sup>5</sup> *Amer. J. Pharm.*, 1907, 79, 151-156; *The Analyst*, 1907, 32, 215.

<sup>6</sup> *J. Ind. and Eng. Chem.*, 1914, 4, 665-669; *The Analyst*, 1914, 39, 433.

<sup>7</sup> *J. Soc. Chem. Ind.*, 1911, 30, 398; *The Analyst*, 1911, 36, 294.



for calculating the results, owing to the difficulty of determining when an excess has been added, and it is therefore necessary to determine the amount of quinone chlorimine formed, after addition of excess of hypochlorite and removal of free chlorine from solution. In the absence of free chlorine, the reaction between the quinone compound and hydriodic acid affords a convenient means of determining this. The reaction is the reverse of that given above, four atoms of iodine being liberated by each molecule of quinone chlorimine, and *p*-aminophenol being re-formed.

As no reagent was found which will combine with the excess of free chlorine without also decomposing the chlorimine, and boiling is out of the question owing to the volatility and instability of the latter in hot solutions, the chlorine must be removed by blowing a current of air through the solution. Experiments showed that chlorine is fairly rapidly removed by this means, 100 Cc. of a saturated aqueous solution of this gas losing 98 per cent. of its strength after five minutes aëration at the rate of 700 to 800 Cc. of air per minute, and becoming practically free from chlorine after fifteen minutes. The quinone chlorimine being also slightly volatile, and tending to decompose on long standing in acid solution, it is necessary to add a small correction to account for this. Any error introduced by the action of the dissolved air on the iodide subsequently added is included in this correction, which averages 1:5 per cent. of the total quinone chlorimine present for an aëration of from fifteen to twenty minutes.

The details of the method finally adopted are shown in the following examples of its application:

*Estimated of p-Aminophenol, p-Phenetidine, etc.*—An amount of an acid solution equivalent to about 0.1 Gm. of the base is measured into a 250 Cc. stoppered bottle and diluted to rather more than 100 Cc.; 5 Cc. of strong hydrochloric acid are added, followed by 10 Cc. of sodium hypochlorite solution (about 0.8 N). The resulting solution should be pure yellow, and not deposit yellow flocks. Air is now blown through at a brisk rate for fifteen minutes, in which time all chlorine will have been removed, 2.5 Gm. of potassium iodide are added, and the solution allowed to stand for at least five minutes, as the reduction is rather slow. The liberated iodine is then titrated with *N*/10 thiosulphate and starch indicator. Any residual blue tint shows that reduction has not been complete.

Each Cc. of *N*/10 thiosulphate is equivalent to 0.00273 Gm. of

*p*-aminophenol, or 0.00343 Gm. of *p*-phenetidine. The result is multiplied by the factor 1.015 to correct for loss during aeration.

*Estimation of Phenacetin.*—One Gm. of phenacetin is boiled for two hours with a mixture of 25 Cc. strong hydrochloric acid (1.16) and 15 Cc. water in a small flask fitted with an air condenser. After cooling, the solution is diluted to some definite volume, and an aliquot representing 0.2 Gm. phenacetin is taken for estimation exactly as above.

Each Cc. of *N*/10 thiosulphate is equivalent to 0.00448 Gm. of phenacetin. A large number of samples of commercially pure phenacetin, examined as above, gave figures ranging from 99.2 to 100.2 per cent.

*Estimation of Phenacetin in Admixture.*—The following experiments were made on mixtures of phenacetin with caffeine citrate, salol, and acetanilide respectively:

*With Caffeine Citrate.*—A mixture of 0.8 Gm. phenacetin with 0.4 Gm. caffeine citrate was treated exactly as for phenacetin. The results were slightly high, owing to formation of a small amount of some substance from the caffeine citrate which liberated iodine from hydriodic acid. The percentage of phenacetin calculated out 68.5 and 68.7, instead of 66.7 required by theory. No correction for the volatility of the quinone chlorimine was made in these cases, the error already mentioned more than compensating for loss by this means.

*With Salol.*—A mixture of equal parts of phenacetin and salol (0.5 Gm. of each) was dissolved in 20 Cc. 10 per cent. sodium hydroxide, and warmed on the steam-bath for fifteen minutes to hydrolyze the salol; 40 Cc. of strong hydrochloric acid were then added, and the mixture boiled for two hours. The hydrolyzed solution was shaken with ether to remove salicylic acid and phenol, and the chlorination and titration carried out in the usual manner. The amount of phenacetin found was 49.3 per cent. It was found necessary to remove the products of hydrolysis of salol before adding the hypochlorite, as the precipitates they formed with this reagent held back chlorine and caused high results to be obtained.

*With Acetanilide.*—Mixtures of acetanilide and phenacetin cannot be analyzed without first removing the acetanilide, as the aniline produced from this substance forms an oily precipitate which apparently retains free chlorine.

*Estimation of other p-Phenetidine or p-Aminophenol Deriva-*

*tives*.—Lactophenin (lactyl-*p*-phenetidine) and salophen (salicylic ester of acetyl-*p*-aminophenol) were both estimated after hydrolysis in exactly the same manner as phenacetin, lactophenin giving 99.3 per cent. and salophen 100.4 per cent., after adding the correction previously mentioned.

*Analysis of Photographic Developers*.—In addition to the medicinal substances already mentioned, there are several *p*-aminophenol derivatives largely used in photography as developers, which may be estimated in the same manner. For instance, in a developer of the rhodinal type, the proportion of *p*-aminophenol may be quickly found by direct treatment of the acidified solution, the sulphite present being oxidized by the excess of chlorine added.

In the case of metol (methyl-*p*-aminophenol sulphate) it is interesting to note that, owing to the presence of the methyl group in the amino-group, no chlorination of the latter takes place, although a quinone derivative is formed. The reaction is probably



Consequently, in the subsequent oxidation of hydriodic acid, only two atoms of iodine are liberated per molecule instead of four, as in the case of *p*-aminophenol. The reaction therefore provides a simple means of distinguishing between metol and "metol substitutes," as all the substitutes that I have examined have proved to be either *p*-aminophenol or *p*-aminocresol salts, none of them showing evidence of the presence of a methyl group substituted in the amino group, when tested by the quinone chlorimine method.

I desire to express by thanks to Messrs. Boots' Pure Drug Co., in whose laboratories the above work was carried out.

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## AN IODINE FACTORY IN EASTERN SIBERIA.<sup>1</sup>

BY DOROTHY F. FINDLAY, M.P.S.,

VLADIVOSTOK, E. SIBERIA.

We came upon it on the edge of a beautiful little bay, about 200 miles north of Vladivostok, surrounded by immense bush-covered hills. Among the vastness of the Siberian scenery the little iodine factory looked very insignificant—a big chimney, a low red brick

<sup>1</sup> Reprinted from *The Pharmaceutical Journal and Pharmacist*, January, 1919.



building, mounds of kelp along the beach, and a distinct medicinal odor in the immediate vicinity. All around on three sides, stretching for miles and miles, hill upon hill, mountain upon mountain, and on the fourth side the ocean. We had come overland, through the big government coal mines of Soo-chan, leaving the mines at day-break, travelling by talaga (Chinese carts) to the coast. The weekly boat to Vladivostok was due in that night, and we intended returning by her. The little village is quite a center for outward and inward passengers, chiefly farmers taking their cattle and produce into town. There is no accommodation for passengers whatsoever, no hotel, restaurant, or waiting-room. The cattle are all deposited on the beach, and the travellers—Chinese, Koreans and some Russians—squat around. They often wait there for hours, as they must arrive by daylight and the boat seldom gets in before 2 A.M. The village—though it can scarcely be called such—consists of the factory and not more than six Russian houses, the remainder being Chinese and Korean huts.

It was pleasant to find something to while away the hours of waiting. The manager of the factory being away, we were shown round by a post-graduate student, who explained every process to us in voluble Russian. It is not necessary to go into details of the manufacture. Newth gives the same process as the one adopted at this factory; suffice it to say that everything is done on the simplest lines. Chinese junks (sailing boats) go out and rake in the seaweed, which is carried up to the top of the beach, stacked in piles, and burnt on the spot, at a stone's throw from the factory. The ash is wheeled straight into the tanks, lixiviated with water in the usual way. Potassium and sodium salts are also made in these works, but their specialty is the pure element. When we had finished our tour we were taken into the laboratory, a large case was unlocked, and with huge pride four large bottles of pure iodine were taken out, each holding 5 kilograms. I had never seen the beautiful glistening scales in such large quantities. This comparatively small case contained the produce of three weeks' work, but was satisfactory, considering the present price of iodine. The head chemist was an ancient Japanese; Japanese chemistry books lined the book-shelves. It was nearly three years since I had been in a laboratory, and this small one was very homely. I went round reading the formulæ on the bottles of the reagents to see if I remembered them. A volumetric analysis was in process at one bench, the pipette

was full of pot. perman. solution; it brought back pleasant memories of a little room behind the shop of a lady chemist, where I did most of my work for the Minor. But it was getting dark, the assistant manager was waiting to shut up and go home. We had nothing so cheerful to look forward to, and it was coming on to rain.

We took shelter under a rock for some hours, and ate our supper of eggs and stale bread and butter brought with us from the day before. At ten o'clock we were rather wet, and went down to the pier to inquire if the boat was soon due. Nobody knew, which is usually the case in Russia. After hanging round for another hour the postman came down with the news that the boat had not left Vladivostok, and there was something wrong with the engine. Our only way home was by talaga, the way we had come, and no driver would think of starting off in the deluge which was now beginning, the rain coming down in bucketfuls at a time. We rushed to the nearest Korean hut for shelter, and were shown into a tiny room about four yards square, where already about a dozen people were waiting. The place had no ventilation, except the door, and was lighted by a glimmer from an evil-smelling oil lamp. It was unpleasant for us, but far more so for the poor farmers who in many cases had come two or three days' journey with their cattle. Only in Russia would people have taken things so placidly. We ourselves were not in at all a good temper. Those who have only ridden in carts along even the worst English road cannot imagine the discomfort of travelling in Chinese carts. These consist of shafts, four wheels, and some planks of wood laid across the axles. The roads are only rough tracks, full of boulders and ruts; there are many streams to cross, and the bridges usually consist of faggots laid across, and the jolting over these without springs is indescribable, and after the heavy rain the roads would be nearly a foot deep in mud, and we should get splashed up to our necks. It was a weird night: inside—the flickerings of the smelly lamp, the alternate arguments and snorings of the farmers, the pest of all creeping things which soon found their way from the walls on to the nearest human body; outside—the rain pouring down, the neighing of horses, and the lowing of cattle. At 3 A.M. the rain somewhat abated and we managed to persuade a driver to take us as far as a village ten miles on the road. With some difficulty he found his own horses, and we left the stifling atmosphere of the hut for the damp dark air outside, with its slight taint of iodine. We splashed through the

mud to our hard seats, and drove into the darkness of the mountain side.

## STROPHANTHUS SEMINA, B.P.<sup>1</sup>

BY E. M. HOLMES, F.L.S.

The commercial history of the strophanthus seed of commerce since its introduction into medicine in 1886, was given by me in 1896,<sup>2</sup> and it was then pointed out that the seeds met with in commerce were invariably mixed with the seeds of other species in varying proportions, and that the seeds of *Strophanthus Courmontii* and its varieties were practically impossible to separate by the naked eye, so that unless the seeds were sent in pods it would be impossible to comply with the Pharmacopœia directions, and use the seeds of *S. Kombe* only.

But although these facts were published in 1906, and illustrations of the difference in the leaves and flowers and seeds of *S. Courmontii* were given with *Pharm. Journ.*, 4, XII., p. 486, the B.P. did not in 1914 direct that the seeds should be kept in their pericarps until required for use, as is ordered in the case of cardamom seeds. For some years past it has been impossible to obtain pure seed of *S. Kombe* in commerce.

The objection has been raised by drug brokers that the weight of the pods adds much to the freight, and that the buyers object to giving more than 3s. 6d. per lb. for the seeds of *S. Kombe*, because other strophanthus seeds can be bought at that price. (But the first importation was entirely of pods, and was purchased by Messrs. Burroughs and Wellcome at a good price.) The result has been that a large number of strophanthus seeds of various species and of unknown medicinal properties have entered into commerce and have been sold as "strophanthus" seeds, dealers being apparently satisfied if there are enough Kombe seed mixed with them "to swear by," and in some cases purposely mixing different lots. The danger of this carelessness about one of the most valuable heart remedies, when given in a proper dose, but which is also a dangerous heart poison in too large a dose, is leading to results that might easily prove disas-

<sup>1</sup> Reprinted from *The Pharmaceutical Journal and Pharmacist*, January, 1919.

<sup>2</sup> *Pharm. Journ.*, 4, XXII, p. 312.



trous. During last week a pharmacist asked me for an opinion on a case that came within his daily work. A patient brought in a prescription of a London physician, ordering *three times the maximum dose* of the B.P. tincture (without any indication that the physician was aware of the fact). The chemist hoped to be able to telegraph to the doctor, and made an excuse that it would take time to prepare, but the customer said he must have it at once, as it was a severe case of heart disease and the dose was wanted immediately. The chemist had to consult a neighboring doctor, who advised him not to give more than the maximum B.P. dose.

It is quite obvious that if one pharmacist (retail or wholesale) has a different sample of seed to work with, there is no certainty under present conditions that the same prescription prepared at different shops will be of the same strength, and the relief that the medical man has a right to expect for his patient cannot be depended upon.

The question of price of the seed ought not to enter into the question. In the case of powerful drugs like *strophanthus*, *aconite*, and *digitalis*, used for serious diseases requiring prompt measures, it is important either that the Food and Drug Act should be strictly applied to punish those using adulterated or mixed samples, or that a government inspector of vegetable drugs should be appointed to prevent such important remedies, if adulterated or diluted with other species, from entering into commerce. In view of the limited geographical range of *S. Kombe*, it might be well to order the use of *S. hispidus* instead, as it is much more widely spread and more easily obtained, and is the only other known species that gives the green reaction of sulphuric acid with *strophanthus* seed, indicating the presence of *strophanthin*.

*Aconite*, which affords a similar instance of possible danger to patients, has already fallen somewhat into disuse for internal use, owing to the substitute of *Aconitum paniculatum* for the preparation of extract, and of Japanese roots not derived from *A. Napellus*, or of German roots of mixed species, for tincture, since these have not the same physiological action, and indeed, contain different alkaloids. These roots, costing half the price of good English root of *Aconitum Napellus*, have practically stopped cultivation in this country, and although during the war it has risen to a price that would pay for its cultivation, the uncertainty of the price being kept up after the war has not led to cultivation on a commercial scale.

The small quantities grown by lady herbalists since the war commenced in 1914, so far as my examination of them has gone, only in two cases proved to be genuine *A. Napellus*, so that even the small amount of "English aconite" in commerce at present is of doubtful origin. Fortunately homœopathists in this country are more careful to secure the genuine species and a definite variety of it, and by preparing the tincture from the fresh plant collected in May, when the characters that distinguish the flower can be seen, their "mother" tincture can generally be depended upon to give promptly the physiological action of the plant. I would suggest that in the next pharmacopœia the tincture of *Aconitum Napellus* should be prepared from the fresh plant, collected in May and grown in Great Britain. This would exclude nearly all the other species grown in gardens, since they flower later, and the plant if collected as soon as the flowers begin to expand would show the shallow helmet characteristic of the best form of *A. Napellus*.

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## BOOK REVIEWS.

SQUIBB'S ATLAS OF THE OFFICIAL DRUGS, by William Mansfield, A.M., Phar.D. Published by E. R. Squibb & Sons, New York, N. Y.

While recognizing the fact that this book has been prepared and distributed to a large extent as a means of advertising the products of a pharmaceutical manufacturing house, we appreciate also that in this publication a distinct service has been performed to pharmacy. A working knowledge of drugs is far too limited among those whose duty it is to supply medicines and who should be well equipped with such information. Any work that will encourage the study of pharmacognosy and stimulate the pharmacists and the students of pharmacy to acquire a more intimate and accurate knowledge of the materia medica is a welcome addition to the pharmacist's library and this book is well calculated to render such a service.

The intent of the author to present in a practical manner what he terms "the living materia medica, the standardized drugs of the United States Pharmacopœia and of the National Formulary" is well carried out. We cannot, however, refrain from criticizing the language of this statement as there are many articles of materia

medica which from the frequency of use are surely "living materia medica" that are not included in the present editions of either the U. S. P. or N. F. Moreover, these official promulgations have "standardized" comparatively few of the official drugs of vegetable or animal origin, in that their therapeutic activity is determined by chemical assay of their active medicinal constituents or by a physiological assay of their potency.

While agreeing with the statement in the preface that "all that is mentioned in Squibb's Atlas is of worth," we are not prepared to endorse the initial laudatory statement therein that "Squibb's Atlas of the Official Drugs is a complete, up-to-date, trustworthy handbook on pharmacognosy." As a matter of fact, "a complete, up-to-date and trustworthy handbook on pharmacognosy" has not yet been published in the English language.

The classification of the contents is simple and excellent and the treatment of the macroscopic characters of the materia medica considered is concise, to the point and in the main quite satisfactory. The terms used in the descriptions are necessarily technical, but are free from the ultra scientific phraseology that has too frequently confused the students of pharmacognosy. "Hackly" is a good English word and well selected to define "a fracture with a sharp and jagged surface." We note, however, that in speaking of fracture on page 9 the word "*concordal*" is used, instead of *conchoidal*, to define a fracture with curved surface and that in numerous other places throughout the pages the same error occurs.

The photographic illustrations of crude drugs and of trade or imported packages of some of these, are good pictures of type specimens as the drugs should appear in commerce. These pictures are the most valuable feature of the book and generally well represent the macroscopic appearances. As a means of presenting the histological characteristics, these illustrations cannot be looked upon as a success. For example, the size of the pictures of the cross sections of Mexican sarsaparilla and of triticum preclude anything like a differentiation of the tissues present in these. Modern pharmacognosy is concerned equally with the study of the microscopic as well as the macroscopic characteristics of drugs as a clear understanding of both is essential.

G. M. B.



AN ADVANCED COURSE IN QUANTITATIVE ANALYSIS WITH EXPLANATORY NOTES, by Henry Fay, Ph.D., D.Sc., Professor of Analytical Chemistry in the Massachusetts Institute of Technology. First Edition, v + 11 pages. New York, John Wiley and Sons, Inc.; London, Chapman and Hall, Ltd. Cloth, \$1.25 net.

Intended primarily for students of the above mentioned institution who have finished the introductory course in "Qualitative Analysis," the title unfortunately does not enable one to judge the contents which are as follows:

Part I—Mineral Analysis:

Sampling for Analysis; Determination of Silica in Decomposable and Refractory Silicates, of Potassium and Sodium in Silicates; Analysis of Spathic Iron Ore; Determination of Sulphur in Pyrite, of Titanium in Titanium Iron Ore; Iodometric Determination of Copper; and Proximate Analysis of Coal.

Part II—Metal Analysis:

Phosphor-Bronze; Carbon, Manganese, Phosphorus, Sulphur, Copper, Nickel, Chromium, Tungsten, and Vanadium in Steel; Phosphorus, Sulphur and Silicon in Cast Iron.

Concluding with Tables of Atomic Weights and Logarithms (4 place) and the Index.

Methods of analysis are followed by a series of explanatory notes in which attention is directed to the reasons for prescribed procedures, to errors that are possible, to advantages which one method may have over another, to the influence of certain constituents upon the properties of metals or alloys and to literature references.

The excellent plan followed in this book could, with advantage, be used in books taking up other lines of quantitative analysis. A close inspection of the book has disclosed but few necessary corrections or suggestions. On page 28 the coefficient in the formula of water is transposed. On page 110 (index) magnesium is proper where printed, but in the text, pages 18–19, giving directions for certain manipulations, no reference is made to the fact that magnesium is being determined nor is even the composition of the final product given, except in the explanatory notes on page 27. Manganese is not given in the index, but it was found that the last two lines under magnesium related to manganese.

FRANK X. MOERK.

ESSENTIALS OF PHARMACY, by L. E. Sayre, Dean and Professor of Pharmacy and Materia Medica, and L. D. Havenhill, Professor of Pharmaceutical Chemistry, of the School of Pharmacy, University of Kansas. Cloth, 12mo, 466 pages. Published by W. D. Saunders, Philadelphia.

This publication, an enlargement of an earlier edition, consists of a concise assemblage of pharmaceutical facts. The first section deals with general processes and definitions, the official inorganic chemicals and related subjects are next considered, then the organic chemicals of the Pharmacopœia and N. F., and lastly, the pharmaceutical preparations of both books.

The facts are condensed and an effort has been made to place before the student only the most essential considerations. The arrangement is such that the chief value would seem to be for purposes of a review by students who have already been well grounded in the subjects presented, since these are presented alphabetically and without any consideration of their relation to each other. As an illustration, the unrelated subjects of "elutriation," "enfleurage," and "evaporation," follow each other because of their alphabetical order.

This book would therefore seem to find its chief use for the graduate who is reviewing the "essentials" of pharmacy, or for a student who is preparing for examinations. The typographical arrangement is excellent and the text has evidently been carefully prepared.

E. F. C.

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## OBITUARY.

### JOHN F. PATTON.

John F. Patton, former president of the American Pharmaceutical Association, died at his home in York, Pa., on Monday evening, March 17, after only a few hours illness, his death being attributed to heart trouble. Although in his eightieth year, he had enjoyed good health and up to the day of his decease was actively engaged in his pharmacy.

John F. Patton was born in Lower Windsor Township, York County, Pa., on December 15, 1839. He was the fourth son of Ebenezer and Rebecca (Smith) Patton. His grandparents were

sturdy Irish immigrants who settled in Chester County, Pa., in 1780, and raised a family of fifteen children, twelve boys and three girls.

John F. Patton received his education in the public schools and in 1853 he came to York and engaged as a clerk in a dry goods store. In 1856, he decided to take up the study of the drug business and engaged with Dr. Jacob Hay, Sr. From 1859 to 1866 he was in the employ of the wholesale drug firm of Thomsen & Block, Baltimore, Md. In 1869, he opened a small store for himself on the north side of West Market Street, York. He soon prospered and in 1873 he removed to a larger store. His efforts and ability were rewarded with a constantly increasing business and in 1884 he built a three-story brick building with what, at that time, was considered a large store. Before his new store was completed, his drug stock was almost entirely ruined by the disastrous flood in June of that year and Mr. Patton had a narrow escape from death. Up to the time of his decease, he continued in the drug business at this location and enjoyed a wide circle of friends and customers.

John F. Patton never married. He was a member of St. Paul's Lutheran Church. He was noted for his quiet, yet effective service, that won the esteem and confidence of all with whom he came in contact. He always took an active interest in the pharmaceutical organizations and for many years faithfully attended the meetings of the Pennsylvania Pharmaceutical Association and the American Pharmaceutical Association, and the appreciation of his work in behalf of his chosen profession is shown by the fact that he was elected to the presidency of the State Association in 1891, and in 1900 was elected President of the American Pharmaceutical Association and presided over the meeting of that body held at St. Louis in 1901.

### JAMES OSCAR BURGE.

James Oscar Burge died at his home in Nashville, Tenn., on February 6, 1919, in his seventy-first year. He was born near Bowling Green, Kentucky, on March 27, 1848. He was graduated from the Philadelphia College of Pharmacy in 1876 with honor, having passed a meritorious examination and ranking seventh in a class containing many who subsequently won distinction in the profession of pharmacy. Among these we may mention Professors Henry Trimble and C. S. N. Hallberg. The subject of Mr. Burge's



thesis was "The Chemical Laboratory," and throughout his many years of pharmaceutical experience his preference was well known to be for chemical and laboratory work.

He engaged in the drug business in Bowling Green, Ky., and later in Nashville, being interested in a number of drugstores in these localities. In recent years he was associated with several wholesale drug and chemical companies, his most recent venture being the Gattis Chemical Co. which he organized in connection with his son, J. O. Burge, Jr.

He joined the American Pharmaceutical Association in 1878 and was elected honorary president in 1916-1917. He always took an active part in matters pharmaceutical and usually attended the meetings of the A. Ph. A. He was one of the best known pharmacists in the country as well as a leading exponent of pharmacy in Tennessee. He was the president of the Nashville Branch of the A. Ph. A.

He took an active interest in the civic matters of the city and also in the religious circles and was a member of the Edgefield Baptist Church.

#### DR. NATHAN C. SCHAEFFER.

Dr. Nathan C. Schaeffer, Superintendent of Public Instruction in Pennsylvania, died at his home in Lancaster, Pa., on Saturday evening, March 15, after a lingering illness, at the age of 70 years. He was born in Maxatawny Township, Berks County, Pa., on February 3, 1849. He was educated at the Franklin and Marshall College, graduating therefrom in 1867 and later received the degree of doctor of philosophy from his alma mater.

He likewise attended several of the German universities and also studied at the Theological Seminary of the Reformed Church. Dickinson College conferred upon him the degree of doctor of divinity and doctor of laws in 1904.

His literary work was mainly on educational and Biblical subjects. He was a professor at Franklin and Marshall College from 1875 to 1877, when he resigned to accept the position of principal of the Keystone State Normal School. In 1893 he was appointed State Superintendent of Public Instruction, and retained this position throughout the several administrations until the time of his decease. He was the chairman of the commission that drafted the present Pennsylvania State School Code.

## PROFESSOR JOSEPH KAHN.

Professor Joseph Kahn, Phar.D., of the Brooklyn College of Pharmacy, in which he held the chair of chemistry, died suddenly at that college on March 3, and he was buried with impressive ceremony therefrom on Wednesday, March 5.

He was a Russian by birth and about forty-five years of age. Emigrating to this country as a poor immigrant lad, he succeeded in obtaining an education by perseverance and a determined financial struggle. With few friends to divert his attention, he devoted himself to the study of pharmacy and later to the mastering of the chemical sciences. By the dint of his efforts he won recognition, position, and the esteem of many with whom as a teacher and member of the pharmaceutical societies he came in contact. The contributions that he had made to pharmaceutical literature evidenced his ability for research and the possibility of a bright professional career.

## HENRY KOOPMAN.

Word has been received in this country of the death in Sweden on January 5 of Henry Koopman, formerly of McKesson & Robbins, and well known to retail druggists throughout the United States. Mr. Koopman joined McKesson & Robbins in 1875 and was for thirty-eight years active in the development of its business. Among some of his other activities, Mr. Koopman organized the Spanish Department of McKesson & Robbins, now one of the large flourishing departments of that organization. In April, 1913, on account of heart trouble, Mr. Koopman retired, by the advice of his physicians, and went to Sweden, the home of his wife, where he has since resided, and where, as just advised, he died.

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NEWS ITEMS AND PERSONAL NOTES.

THE HARRISON NARCOTIC LAW UPHOLD.—In two recent decisions the U. S. Supreme Court has sustained the constitutionality of the act approved December 17, 1914, and commonly called the Harrison Act. The first decision was based upon the case of C. T. Doremus, a Texas physician, who was accused of selling a quantity

of heroin tablets to a "dope fiend" for use as an habitual user and further that the sale was not on a written order on an official narcotic order in accordance with the provisions of the law, thereby violating sections 1 and 2 of the Act.

The contention of the defendant was that section 2 was an interference with the police powers of the states and was not related to the collection of excise taxes. By a majority decision the validity of the measure was affirmed because it opened a possible way for dealings in narcotic drugs without the payment of the revenue tax.

The second decision was based upon the case of Dr. Webb, a physician, and one Goldbaum, a druggist of Memphis, Tenn. The former prescribed morphine for the purpose of habitual use to "dope fiends" and the latter had filled over 4,000 such prescriptions; the specific case cited was a sale to a non-resident of the state of ten so-called prescriptions, at one time, for one drachm each of morphine. The decision upholds the constitutionality of the provision that the sales of these narcotic drugs must be made only on the official order forms or on registered physicians' prescriptions given in good faith in the treatment of disease or to effect a cure.

The Chief Justice and three other members of the Supreme Court dissented from these opinions.

LEHN AND FINK PROVIDE LARGER FACILITIES FOR BUSINESS.—Messrs. Lehn and Fink, Inc., the well-known wholesale druggists and manufacturing pharmacists of New York City, announce that they have completed arrangements for the erection of a new six-story building to be located at Greenwich, Morton and Barrow Streets. As soon as the new building is completed they will remove from their present location, 118-120 William Street, and their expectation is to have at least three times the space that they have available at the present time. The firm was organized in 1874 and was composed of gentlemen who had a large acquaintance with the drug trade and who were well equipped and possessed a broad knowledge of the drug markets of the world. The successful development of a line of pharmaceutical specialties contributed materially to their business growth which has necessitated the acquisition of new and larger quarters.

PRINCIPLES OF THE U. S. P. REVISION TO BE DISCUSSED.—Dr. Wortley F. Rudd, chairman of the Section on Education and Legis-



lation of the A. Ph. A., announces that it is proposed to devote a portion of one session of that Section at the New York Meeting of the association in August to a discussion of the general principles that should obtain in the next revision of the U. S. P. Constructive papers, suggestions and discussions will be the timely object in view.

THE INTER-RACIAL COUNCIL AND ITS WORK.—This organization, of which Coleman du Pont is chairman and Philip T. Dodge vice-chairman, has opened offices at 120 Broadway, New York City, and has engaged upon an important educational programme of Americanization. In a recent communication attention is directed to the importance of developing "A Foreign Market at Home." It is shown therein that there are in America fifteen million foreign-born, and including those of foreign parentage, it is estimated that there are thirty-three million who should be cultivated as purchasers of American-made wares, instead of encouraging the existing preference for the familiar production of their native countries.

The campaign is to make the thrifty foreigner a good customer for American goods; to teach him the merits of such and to encourage him to live in truly American style and ways. The purpose is to further this movement in various ways, not the least important of which will be by utilizing advertising space in the 1,146 American papers printed in foreign languages in the United States (excluding the German, which number 483) and 85 magazines, many of which have a wide circulation and exert great influence. These are to be made "trade missionaries" to aid in the Americanization plans contemplated.

CHANGES IN THE MANAGEMENT OF H. K. MULFORD CO.—At a recent meeting of the directorate, Mr. K. K. Mulford resigned as vice-president of the corporation and Mr. Hilson H. White was elected to fill this responsible position. Mr. White was born in Scotland and received his education in several colleges in Scotland and England. He was engaged for some years in one of the large pharmacies in Toronto, Canada.

Having accepted a position as a travelling salesman with the H. K. Mulford Co., he enthusiastically devoted his energies to what was to him a congenial opportunity for expansion. His success and marked ability won recognition and in 1910 he was made general sales manager for the company. Advancement has been rapid, and

in 1915 he was elected a director and in 1918 was made assistant to the president, and now has the further honor of being made vice-president.

Mr. R. L. Derr, who for some years past has been the manager of the Chicago branch of the H. K. Mulford Co., has been promoted to the position of supervisor of the various branches of the company and has removed to the home office in Philadelphia to assume charge of his new duties.

DR. A. PARKER HITCHENS WITH ELI LILLY AND COMPANY.—Dr. A. Parker Hitchens, who has a national reputation as one of America's leading bacteriologists, has accepted an appointment in the management of the Biological Laboratories of the Eli Lilly Company of Indianapolis.

Dr. Hitchens is the secretary of the American Society of Bacteriologists and is the editor of the publication of that organization *Abstract of Bacteriology*. During the war he entered the Army Medical Service and was commissioned as a major and assigned to duty in the Army Medical School in Washington and devoted most of his time to the study of the bacteriologic problems associated with influenza. Upon discharge from the active service, he was commissioned a lieutenant-colonel in the Medical Reserve Corps.

CHANGES IN THE SCIENTIFIC STAFF OF BURROUGHS WELLCOME RESEARCH LABORATORIES.—Dr. T. A. Henry, late superintendent of the laboratories at the Imperial Institute, London, has been appointed director of the Wellcome Chemical Research Laboratories, London.

Dr. F. L. Pyman, the former director of these laboratories, has accepted the professorship of technological chemistry in the Manchester Municipal College of Technology, and in the University of Manchester.

THE REMINGTON MEMORIAL HONOR MEDAL IN PHARMACY AWARDED.—The first award of the Remington Honor Medal, provided by the New York Branch of the American Pharmaceutical Association, is to be made this year. The Committee on the Award have selected Dr. James H. Beal, former president of the American Pharmaceutical Association as the first recipient of this distinguished honor.

Dr. Beal's work in behalf of pharmacy is too well known to require any recounting at the present time. As general secretary of the A. Ph. A. and as the first editor of the *Journal of the American Pharmaceutical Association*, as member and president of the National Drug Trade Conference, as chairman of the Commission on Proprietary Medicines, as chairman of the Board of Trustees of the U. S. Pharmacopœial Convention, and in many other ways has he shown his exceptional ability and his earnest efforts in behalf of the profession. The honor is deserved and the distinction accorded is fully merited.



# THE AMERICAN JOURNAL OF PHARMACY

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MAY, 1919

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✓EDITORIAL.

## THE REGENERATION OF THE MEDICAL PRACTICES.

Following the greatest of all wars, the world is brought to a realization of the fact that it is confronted by many and most momentous problems. The battles of peace of this post-bellum period of world re-formation, bid fair to have quite as important a bearing upon the destinies of nations and in determining the progress of the world as did the gigantic battles of the war.

Out of this great war and the resulting occurrences there should come, and must come, a better world with a clearer understanding of the just rights and privileges and also the duties of each individual and of each class of citizens as well as of each aggregate of citizens that are deemed a nation. If this be not so, then the victory of this great struggle will be meaningless as guaranteeing the betterment of world conditions. The enormous loss of life entailed, the unprecedented devastation and destruction of property, the untold wealth poured out to attain the war's termination and the innumerable sacrifices made by men and women in all civilized countries, will otherwise all have been very largely in vain.

The problems of this period are so numerous, so far reaching and so important that they cannot be compared with the reconstruction periods following previous wars. They portend the birth of a new order of things, a new era, of actual regeneration for many vocations and for some nations.

Democracy means that each self respecting, intelligent, citizen must assume his full share of responsibility not only for national government but also for national progress, the social, educational, industrial and financial development of his country. With the

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added responsibilities will come improved opportunities for advancement.

Throughout the civilized world, the medical profession as a body generally commands respect and confidence and in the readjustment of industrial, social and political conditions that is now in process, medicine should assume its full responsibility and a position of active leadership.

Modern medical practice differentiates the duties of the physician, the surgeon, the dentist, the veterinary doctor and the pharmacist. Each of these have a distinct professional field and perform separate and necessary services to society. Society relies upon each of these branches and is dependent upon each for faithful performance of duty and, despite the false ideas held by some, they are interdependent upon each other.

Each of these branches of medical practice is based upon a collegiate education in the sciences that, with the granting of a professional degree, assumes that the standing and future actions will be ethical and with proper regard for the professional status of each other and the progress and elevation of all. Yet none of these branches of medical practice have been free from severe criticism because of the continuous and flagrant breaches of professionalism. The commercial spirit has dominated them all to such an extent that only too often have professional ideals become merely a secondary consideration.

They are all honeycombed by false practices and jealousies that are foreign to their codes of ethics. Questionable cults, quackery and chicanery have been engrafted upon medicine and fake remedies and "cure alls" of the vilest type and the numerous queer side lines have queered pharmacy. The misrepresentations and the misleading advertisements of the newspapers, and even appearing in some of our so-called professional journals, have injuriously affected all branches of medical practice. It does not make the violation of the code of ethics any the less, nor does it improve matters the least that the dispensing physician lays the blame for his unethical practices at the door of the counter prescribing apothecary or that the latter attempts to excuse himself because of the former's errors. Such crimination and recrimination is a useless exhibition of a spirit unworthy of professional men and these have no influence whatever in the correction of the faults of either.

In the present attitude of the world for exact justice, for a read-

justment of social conditions, and the demand for better professional service and with the shortage of medical practitioners, there is afforded at this time an unusual opportunity for reform in the medical practices. The various branches of the medical profession should realize that this is the golden opportunity for them to combine their efforts for the eradication of long standing evils and jealousies. Such a regeneration is a need of the time and is essential to the proper advancement of the ethical practice of medicine. It is not a new principle that we are proposing in advocating that selfishness shall cease to be the controlling influence and that in the future these practices shall be swayed by altruistic, yet potential, professionalism. In a recent article Elihu Root declared that "change and growth are the law of life" and this law is applicable to the existence of vocations as well as to that of nations.

Can the leaders in the several medical practices rise to the opportunity and appreciate the possibilities growing out of such a regeneration? It should not be too much to expect of broad minded professional gentlemen that they entertain this proposition with the thought that "the past is behind us, the future is ahead. Let us all strive to make the future better and brighter than the past ever was."

The regeneration advocated is not chimerical but a reformation that is needed and should appeal to all as a perfectly just and feasible proposition. Coöperation will be essential and it must be co-operation of the real earnest and sincere type. It should not be considered at all impractical for the national organizations representing medicine, surgery, dentistry, veterinary medicine and pharmacy each to appoint a representative Committee on Fraternal Relations and to charge these joint committees to act as a commission to define the scope and policy for each branch of medical practice and to study the means of bringing about a closer relation among them and a correlation of their services of eliminating unethical practices and encroachments.

G. M. B.



THE PENNSYLVANIA COLLEGES OF PHARMACY  
ANNOUNCE ADVANCED ENTRANCE  
REQUIREMENTS.

The following is a copy of the official letter addressed to the Pennsylvania Board of Pharmacy, advising the Board of the advances in the preliminary education unanimously agreed to be required of students admitted to the pharmacy course in the three schools located within that State. This evidences the intent of these schools to enforce the agreement adopted at the Indianapolis meeting of the American Conference of Pharmaceutical Faculties.

It is hoped that the example thus set by the Pennsylvania schools in this official notice, will be followed by all the schools of pharmacy located in the United States and that by this means ample information will be conveyed to the pharmacists and to the prospective students in pharmacy so that no hardships will result by reason of insufficient preliminary education on the part of those who wish to enter pharmacy. With such ample notice of intended advances, the pharmacists should see that their assistants have the preliminary education required and that any deficiency is made up by study before applying for admission as a student in a pharmacy school.

PHILADELPHIA COLLEGE OF PHARMACY.

FOUNDED 1821.

145 NORTH TENTH STREET.

April 16, 1919.

DR. L. L. WALTON, *Secretary*,  
PENNA. BOARD OF PHARMACY,  
WILLIAMSPORT, PA.

*Dear Dr. Walton:* At a meeting of the deans of the three colleges of pharmacy in this State, recently held in Philadelphia, it was unanimously decided that the entrance requirements for pharmacy should be advanced in accordance with the agreement of the colleges belonging to the American Conference of Pharmaceutical Faculties.

The following advances in entrance requirements were therefore agreed upon:

For the sessions of 1919-20 and 1920-21, not less than two years of high school or its equivalent.

For the sessions of 1921-22 and 1922-23, not less than three years of high school or its equivalent.

For the sessions of 1923-24 and thereafter, not less than four years of high school or its equivalent.

It is deemed advisable to give advance notice of this step to the Pennsylvania Board of Pharmacy and to the pharmaceutical journals, in order that pharmacists may prepare for these changes by giving intelligent advice to young men and women contemplating the study of pharmacy so that they may be properly prepared when these changes go into effect.

Very truly yours,

J. A. KOCH,

*Dean of the Pittsburgh College of Pharmacy.*

JOHN B. MINEHART,

*Dean of Dept. of Pharmacy of Temple University.*

CHARLES H. LAWALL,

*Dean of the Philadelphia College of Pharmacy.*

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## LIFE AND WORK OF CHARLES TANRET.

BY HENRY KRAEMER.

One of the great names in the Hall of Fame in Pharmacy is that of Charles Tanret, a brilliant French pharmacist, who died after a long illness on July 29, 1917. He was a most unselfish and indefatigable investigator. The pursuit of knowledge was the passion of his life. He was a pharmacist like our own William Procter, Jr. Since the time of Sertürner there has not been a more commanding figure. His life is an inspiration in giving us the nature of the qualities which go to make up true success. Notwithstanding his activities as a retail pharmacist and the exactions on his time in the conduct of a retail drug store, he nevertheless found time to publish nearly 100 papers, representing investigations of a very high order of merit. Tanret will long be remembered for his studies on the active principles of ergot and pomegranate bark. His name will also be connected with the test associated with his name for the detection of albumin, peptones and alkaloids.

Charles Tanret was born on August 10, 1847, in the village of Joinville in Haute-Marne, on the Lorraine side of the boundaries of

the Champagne. His preliminary education, especially in the classics, was of a very high order and formed a very definite imprint on his future career. He was also very fortunate in his apprenticeship in the store of M. Antoine. The latter was a well-educated



CHARLES TANRET

pharmacist and took a great deal of personal interest in Tanret, inviting him to his home, directing his reading and instructing him in the science and art of pharmacy. His employer was a man of magnetic personality and so filled his young pupil and apprentice with enthusiasm and with the possibilities of pharmacy that his sub-



sequent work even astonished his old master. Young Tanret was of an analytical turn of mind and after mastering the simple substances of the French Codex, threw himself into a study of the most complex compounds contained therein. He read diligently and soon found out all that there was to know concerning the preparations and chemicals which were dispensed in this pharmacy.

At the age of twenty-one, he was looking around for a large field and applied for an internship at the hospital of Paris which appointment he received. Tanret's love of country was coeval with his ardor in pursuit of knowledge and when the war of 1870 was declared, he gave up his position at the hospital to fight the invader. He served in the infantry throughout the war and took part in the siege of Paris. At the conclusion of the war, he applied again for the position of internship at the hospital of Paris and, passing the examination, received the appointment the second time. By holding his hospital position he attended the course of instruction at the Collège de France and was particularly impressed with the teachings of Berthelot, for whom he acquired the most profound admiration and who offered him an assistantship. The latter position he could not accept on account of his meager finances and it seems a great pity that one with the initiative and brilliancy of Tanret could not have been permitted to pursue his scientific studies and continue at one of the great schools in Paris. He had won a silver medal at the Ecole de Paris and thought it was not required, presented a thesis entitled "D'Albumine." The work in connection with this dissertation was unusually thorough and contrary to what is usually the case, this thesis was one of his most important scientific contributions and the reactions described bear his name even at the present time.

He had worked himself up to the position of senior interne at the hospital and as the work was becoming more or less routine to him he opened a pharmacy shop at Troyes at the lower end of the la Rue Thiers. I imagine that he was rather happy in this little store, that his clientele was rather small during his first few years, so that it gave him considerable time to pour over the books in the library of his little village. During this time he carefully read all of the volumes of the *Annales de Chimie et de Physique* and the *Comptes rendus de L'Academie des Sceinces*. The more he thought about pharmacy, the more he felt the lure of the study of the active principles of important drugs. His first work which entitles him to

enduring fame was the isolation of the active principles of ergot. Notwithstanding the fact that the experiment required a good deal of money, he with self-denial investigated the nature of the principle and finally succeeded in obtaining a crystalline alkaloid, ergotinine. Upon the completion of this work on ergot, he undertook a study of the alkaloids of pomegranate bark. His success in this study was so great that it attracted wide attention. He isolated four alkaloids, which he named after the French chemist, Pelletier. Furthermore, it was found that the anthelmintic properties of pomegranate were due to these alkaloids and the Academy of Sciences awarded him the Barbier prize.

Tanret was much encouraged by the success of his work and feeling that if he were in a larger city, where the libraries were more comprehensive and the opportunities for scientific research greater, he might accomplish more, he therefore gave up his store at Troyes and moved to Paris. He rented a room on la Rue Denfert-Rochereau street, spending his mornings in investigations and the rest of the day in the laboratory of Berthelot at the Collège de France. These were among his happiest days. His associates were among the master minds of France. He was perfecting himself in analytical methods and acquiring a technique which made him one of the most exacting of investigators. It was while living under these simple conditions that he finished his work on the study of ergot and granatum. It was here also, in collaboration with Villier that he published a paper on the inosite of the leaves of the walnut.

In 1880 he acquired a little drug store at the corner of the Rue de Seze and the Boulevard de la Madeleine. Here his success as an apothecary was almost immediate and one might almost think that as he had tasted enough of the dregs of poverty, he might give up his researches. Not so Tanret. He fitted up a little room in the cellar in which he could steal away from his clientele and continue his scientific investigations. Indeed Tanret's personality was such that his customers looked up to him as a distinguished savant and hesitated to intrude upon him unnecessarily. While occupying this store he published important papers on the active principles in convallaria and vinca, double salts of caffeine, extract of cinchona, terpinol, alkaloids produced by the action of ammonia on glucose, etc. Tanret published 36 papers from the time of graduation from the Collège de France to 1886 and these were assembled in a special pamphlet which he published and distributed among his friends.



In 1886 he gave up his apothecary shop and started a laboratory and an office on la Rue d'Alger. He devoted himself to analytical work and manufacturing on a small scale. He prepared many of the active principles of a high grade of purity. At the Universal Exposition of 1899 he was classed first by the international jury of judges from whom he received the Cross of the Legion of Honor, the only honorary distinction which he was willing to accept during his modest though productive career. In awarding the prize the jury, in the conclusion of their report, said, "By his researches Monsieur Tanret has placed himself in the front rank of analysts. He has succeeded in creating new methods and in bringing into all that he has published an experimental school of the first order."

In 1900 a very great loss befell Tanret in the death of his wife, who had been a companion and an inspiration to him ever since their marriage in 1873. For the time it seemed as though the shock would unnerve him and cause him to drop all of his scientific work. In a little while, however, he recovered himself and through the sympathy of his children took up his studies with renewed energy. During the succeeding years he published some of his most brilliant investigations. They included his work on sugars, the fungi, the glucosides of the bitter orange, the carbohydrates of cereals, the active principles of quebracho, etc. A complete list of Tanret's published papers as well as an excellent biographical sketch will be found in the November number of the *Bulletin de la Société Chimique de France*. There is also a biographical note in the *Bulletin des Sciences Pharmacologiques*, for January-February, 1918.

As has been said earlier Tanret was a patriot of the first order and when the Great World War broke out, although he was an old man, his love for country and self-sacrificing spirit caused him to devote his entire energies for the preservation of the Republic. Immediately he placed the resources of his laboratory in the hands of the medical department, turning over to them his supplies of chloroform, tincture of iodine and other preparations. When the first gas attacks were made by the enemy, he contrived a cotton "antichlore" which he made by the thousands with the aid of his daughter for the troops. His health began to fail in April, 1916, and he was urged to retire to his villa at Sevres, hoping that the change might be of benefit to him. Among the surroundings he loved, his health improved slightly. His mind remained vigorous to the last. Those of his friends who were fortunate enough to visit him were im-



pressed with his breadth of view, his extensive knowledge of French literature, with which he was as familiar as with the master works of the scientists of the world. Early in 1917 the malady with which he was afflicted progressed rapidly, but Tanret's indomitable spirit was almost unconquerable. He continued to work to the very end. The night before his death, he went to his laboratory for the last time. A few hours later he passed quietly away. In accordance with his wishes, the burial service was exceedingly simple and a small company of his intimate friends came to express their sympathies and to do honor to this man of sterling worth whom they had loved. M. Andre, in his biographical memoir, concludes with the following tribute to his memory: "Although inevitable troubles clouded certain portions of his life, one instinctively feels that, on the whole, Tanret was a happy man. He never exhibited the slightest trace of jealousy or envy. He rejoiced in the successes that came to his friends as though they had been his own. He possessed to the depths of his heart a love for his family, devotion to science and loyalty to his friends. Those who came in contact with Tanret will always cherish the memory of that fine face and feel a deep appreciation for the work with which he has embellished French science."

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A NEW METHOD FOR A SEPARATE EXTRACTION OF  
HYDRASTINE AND BERBERINE FROM GOLDEN  
SEAL ON A LARGE SCALE, AND A REVIEW  
STUDY OF THE TWO ALKALOIDS.

BY ELSA SCHMIDT.

I. HYDRASTINE.— $C_{19}H_{15}(O \cdot CH_3)_2O_2N$ . Golden seal (ground for percolation) is moistened with benzol containing a little ammonia and then packed into a percolator and saturated with benzol. The drug is left to macerate for 24 hours, then percolation is started and the drug exhausted with benzol.

The benzol extracts are now shaken out with dilute sulphuric acid (3 per cent.) the acid washings collected and from it the alkaloid is precipitated with ammonia. It may be purified by redissolving and precipitating, or by recrystallization from ethyl alcohol.

*Properties.*—Hydrastine occurs in white or creamy white glistening prisms, or as a white, micro-crystalline powder, and is perma-

nent in air. One gram is soluble in 170 Cc. of alcohol, 1.4 Cc. of chloroform, 175 Cc. of ether, freely in benzol, and almost insoluble in water. The salts of it are yellow. Hydrastine can be prepared synthetically. It is precipitated amorphous from its aqueous solution upon the addition of alkali hydroxides or carbonates, but the precipitate assumes gradually the crystalline form.

*Tests.*—An aqueous 5 per cent. solution made with the aid of dilute hydrochloric acid should not be reddened by chlorine water (absence of and difference from berberine). A 1 per cent. solution in dilute sulphuric acid develops a blue fluorescence if potassium permanganate solution is added; but no fluorescence should be visible before the addition of the reagent. (Distinction from hydrastinine) U. S. P. That is, with oxidizing agents in acid solutions hydrastine yields *hydrastinine* and *opianic acid*, while in alkaline solutions, hemipinic and narcotinic acids are produced.

Froehde's reagent gives with hydrastine a characteristic test. A sage green color appears slowly changing to brownish and then gradually fading.

*Estimation.*—The gravimetric estimation of the U. S. P. is known. Puckner states that the following methods are preferable to those described in the U. S. P. Five grams of the powdered rhizome of *hydrastis canadensis* are treated with 50 Cc. of ether and after standing 10 minutes, 2 Cc. of ammonia are added and the mixture allowed to stand for 30 minutes with frequent agitation. The mixture is then filtered and the residue extracted with a second 50 Cc. of ether. The combined ethereal solution is first shaken with 2 Cc. of dilute hydrochloric acid and 18 Cc. of water, then with 10 Cc. of water containing 5 drops of dilute hydrochloric acid and finally with 10 Cc. of water. The combined aqueous solution is made alkaline with ammonia and extracted three times with 20 Cc. of ether. The ethereal extract is evaporated at ordinary temperature, the residue dried at 98°–100° and weighed.

*Note.*—The author gets the best result by letting 10 Gm. of the powdered drug macerate over night in 100 Cc. of ether and 3 Cc. of ammonia, then taking an aliquot part and continuing as above by using water and acid.

In the case of the fluid extract, 5 Cc. are well shaken with an equal volume of a 20 per cent. solution of potassium iodide and 20 Cc. of water, filtered and the precipitate washed twice by stirring with 5 Cc. of a 1 per cent. solution of potassium iodide, the liquid

being passed through a filter, and then twice with the same solution on the filter. The filtrate and washings are extracted three times with 20 Cc. of ether, the ethereal solution filtered through cotton-wool, evaporated, the residue dried at  $95^{\circ}$ – $98^{\circ}$  and weighed.

2. BERBERINE.—The ground golden seal from which the hydrastine has been removed is dried or drained free from the benzol. It is then saturated with water (hot) acidulated with acetic acid and macerated for a few hours. Percolation is started and the percolate received in a vessel containing a small amount of concentrated hydrochloric acid. Berberine hydrochloride will form immediately and can be filtered out. The berberine hydrochloride thus obtained is rather pure. The first percolate might contain traces of hydrastine. Traces of free chlorine can be removed by washing the precipitate on the filter with a small quantity of water containing only a very small amount of hydrochloric acid.

*Properties.*—Berberine, or its salts, have a persistent bitter taste, and are employed medicinally in doses of 2 to 5 grains. Sixty Grs. have been taken by man without injury but the alkaloid is poisonous to dogs, etc. It dissolves in 4.5 parts of water giving a yellow solution neutral to litmus. It is easily soluble in hot water and alcohol and dissolves in 100 parts of dilute alcohol (Proctor), is slightly soluble in chloroform and benzene, insoluble in ether (separation from hydrastine) and petroleum spirit. According to E. Schmidt<sup>1</sup> berberine has a remarkable tendency to combine with neutral solvents, such as, alcohol, ether, acetone and chloroform to form crystalline compounds. When berberine and chloroform are mixed in molecular proportions they unite to form a beautiful crystalline substance, permanent at  $100^{\circ}$ . This does not appear to be a mere additive product since it is not decomposed by acids simply into berberine and chloroform, but yields decomposition products of the latter. Berberine can also combine with a second molecule of chloroform but this behaves like water of crystallization. Schmidt has also described a compound of berberine with acetone of the formula  $C_{20}H_{17}O_4N$ ,  $C_3H_6O$ .

*Uses.*—Berberine, or its salts, is an excellent tonic and has slightly laxative properties. If administered with hydrastine it will eliminate indigestion caused by the white alkaloid, and being a tonic, will add to the value of hydrastine. It will be found to exert an efficient action upon all abnormal mucous tissues and can be used

<sup>1</sup> *Pharm. Zeit.*, 1887, 32, 542.



where barberry or golden seal is indicated. Its dose is from 2 to 20 grains in powder, or dissolved in water to which a little acetic acid may be added to aid its solution.

*Tests.*—When treated with sodium hydroxide solution, berberine is colored brown, and upon boiling this brown solution a resinous mass separates. On distilling berberine with milk of lime, quinoline is formed. Fusion with potassium hydroxide produces berberic acid  $C_8H_5O_4$ ; and an acid of the composition  $C_8H_5O_5$ .

If treated with nascent hydrogen, berberine is reduced to hydroberberine,  $C_{20}H_{21}O_4N$ . Berberine dissolves in concentrated sulphuric acid with an orange yellow color changing to olive-green on warming. On addition of chlorinated water to a solution of berberine strongly acidified with hydrochloric or sulphuric acid, a zone of bright red color is formed at the zone of junction of the liquids and is still recognizable as a pink coloration in a dilution of 250,000 (Allen). The reaction is destroyed by reducing agents. (Brucine gives a similar indication with chlorine water but the original solution is colorless and the color less permanent than with berberine.) Mayer's reagent gives a precipitate  $B_2H_2HgI_4$ .

*Detection in Plants* (Allen).—Five to 20 Gm. are extracted with alcohol, evaporated, treated with 20 to 40 Cc. of water and filtered through talc. A small portion of the clear filtrate is mixed with a small quantity of a 10 per cent. solution of potassium iodide. If no precipitate is formed no appreciable amount of berberine is present, but if a precipitate is deposited 10 Cc. of the original filtrate are mixed with 1 to 2 Cc. of a 10 per cent. solution of sodium hydroxide, filtered if necessary, heated to 50, treated with 5 Cc. of acetone and allowed to stand. If after two hours no crystals have formed, 30 Cc. of water are added and the solution kept in a cool place over night. In this time crystals will form if 10 Cc. of original solution contained not less than 0.01 Gm. berberine.

The crystals may be identified by dissolving in dilute hydrochloric acid and testing portions of the solution with potassium iodide, potassium dichromate, picric acid, or chlorine water. When no crystals form, although potassium iodide has given a precipitate with the aqueous solution of the extract, 10 or 20 Cc. of the extract are mixed with an excess of a 20 per cent. solution of potassium iodide. The precipitate formed is collected on a filter and washed first with dilute potassium iodide solution and then with water. The filtrate and washings are concentrated to about 2 Cc., treated with a

few drops of sodium hydroxide solution and 1 Cc. of acetone and after standing some hours diluted with an equal bulk of water, good crystals of berberine-acetone will be deposited within 24 hours if 0.0010 Gm. of the alkaloid is present.

A microchemical method of detecting berberine has been described by Bauer.<sup>2</sup> A section of the plant tissue is floated in a few drops of water on a microscope slide, allowed to macerate for a few seconds, warmed with one or two drops of sodium hydroxide solution (10 per cent.) and treated with four or five drops of acetone and covered with a micro-cover glass. The growths of characteristic crystals of berberine-acetone is observed under the microscope in some cases in 5 minutes, while in others several hours are required.

*Estimation.*—Gravimetric method of Gordin. The berberine in an aqueous-alcoholic solution is precipitated with excess of a 10 per cent. solution of potassium iodide, the precipitated iodide washed with a two per cent. solution of KI and transferred with a little water into a flask. After heating to 60°–70° acetone is added to the extent of one-third the volume of the water and the mixture shaken for 10 minutes. Five Cc. of a 10 per cent. solution of sodium hydroxide are then added and the liquid shaken (heating to 50°–60° if necessary) until the yellow hydro-iodide has disappeared. After cooling, the solution is diluted with water to three times its bulk and allowed to stand over night. The berberine-acetone is filtered off, dried first under reduced pressure and then at 105° and weighed. One Gm. of the acetone compound corresponds with 0.853 Gm. of berberine. To correct for the berberine acetone dissolved in the mother liquor 0.0000273 is added per Cc.

*Berberine Hydrochloride.*—By the above mentioned method of manufacturing berberine, the hydrochloride of the alkaloid is obtained. This salt is the easiest obtainable and is very stable. It is not as soluble as the sulphate but as effective, and is readily soluble in boiling water. It is almost insoluble in alcohol or dilute hydrochloric acid and is with difficulty decomposed by bases. Silver-oxide readily decomposes it in solution. *By prolonged exposure at 100° the color changes permanently to an orange color and the salt becomes readily soluble in water with a red color.* This does not contain much if any free chlorine.

*Tests.*—The mixture of the salt with KI changes to a graphite color when treated with a drop of hydrochloric acid and then to a

<sup>2</sup> *Pharm. Zeit.*, 1908, 53, 618.

yellow on adding KOH solution. The salt becomes dark green when mixed with picric acid and treated with sulphuric acid. Its plain solutions are yellow. For properties see under Berberine.

LABORATORIES OF

ALLAIRE, WOODWARD & Co.,

PEORIA, ILL.

## NOTES ON EMETINE HYDROCHLORIDE.

BY GEORGE É. EWE.

### THE PROPORTION OF CEPHÆLINE IN THE EMETINE HYDROCHLORIDE ON THE MARKET.

The manufacture of emetine hydrochloride from ipecac presents the problem of separating emetine alkaloid from the drug, in a condition of comparative freedom from cephæline alkaloid, which also occurs naturally in the drug. Recognizing this problem, the U. S. P. requires the following test to be applied to emetine hydrochloride in order to insure the absence of any considerable proportions of cephæline:

“Dissolve 0.1 Gm. of emetine hydrochloride in 5 mils of distilled water in a separatory funnel, add to the solution 3 mils of sodium hydroxide T. S. and shake it out with 10 mil portions of ether until the residue obtained by evaporating 1 mil of the ethereal liquid when dissolved in 1 drop of diluted hydrochloric acid and 1 mil of distilled water, no longer yields a turbidity with iodine T. S. Now acidulate the aqueous liquid with diluted sulphuric acid, then add ammonia water until alkaline and shake it with 10 mils of ether. Evaporate this ethereal liquid and add to the residue 1 mil of sulphuric acid containing about 0.005 Gm. molybdic acid; no purple color is produced. (Cephæline.)”

When applied to samples of emetine hydrochloride representing the products of five American manufacturers, a pale reddish-purple color, followed rapidly by a brown, and finally a light green was obtained in each case.

The U. S. P. states that “no purple color is produced” and since all of the samples examined gave purple colors, more or less modified and of decided intensity, the amount of cephæline in the samples was



determined quantitatively, in order to ascertain if the proportion present was material in quantity.

The method employed was based on the U. S. P. qualitative test for cephæline modified by starting with 0.6 Gms. of the emetine hydrochloride, increasing all reagents six times when necessary, weighing the cephæline instead of treating it with sulphuric-molybic acid and running a blank correction throughout the method. The larger quantity of emetine hydrochloride was employed in order to obtain an accurately weighable quantity of cephæline.

The quantitative method can be described as follows:

Dissolve 0.6 Gm. in 30 mils of distilled water in a separatory funnel, add to the solution 18 mils of sodium hydroxide T. S. and shake it out with 60-mil portions of ether until the residue obtained by evaporating 1 mil of the ethereal liquid, when dissolved in 1 drop of diluted hydrochloric acid and 1 mil of distilled water, no longer yields a turbidity with iodine T. S. Now acidulate the aqueous liquid with diluted sulphuric acid, then add ammonia water until alkaline and shake it out with 60 mils of ether. Separate and evaporate this ethereal liquid in a tared flask. Dry the residue of cephæline in the flask at 60° C. to constant weight and weigh it as anhydrous cephæline alkaloid. Run a blank correction throughout the method and correct final weight of anhydrous cephæline alkaloid accordingly, if necessary.

Five extractions with ether are usually required before the iodine T. S. fails to yield a turbidity with the extraction, and even after a sixth extraction, a slight turbidity is sometimes obtained. The use of five extractions was adopted in these experiments. A blank correction indicated a necessary deduction of from  $\frac{1}{2}$  to 1 milligram from the weight of anhydrous cephæline alkaloid obtained in the several tests.

The quantitative test was applied to samples of emetine hydrochloride representing the products of five American manufacturers with the following results:

#### ANHYDROUS CEPHÆLINE ALKALOID.

Manufacturer.	Per Cent.
1 .....	1.65
2 .....	3.10
3 .....	2.1
4 .....	0.80
5 .....	2.10

These results indicate:

1. That the U. S. P. test for cephæline, if literally interpreted, would exclude the majority of the emetine hydrochloride on the market.

2. That a material proportion of cephæline is not present in the emetine hydrochloride on the market.

3. A quantitative test along the lines suggested in this paper should be resorted to in the event of an apparently excessive proportion of cephæline being indicated by the U. S. P. limit test.

4. The adoption of an upper limit of 3 per cent. of cephæline in connection with a quantitative test would insure the absence of excessive proportion of cephæline in the emetine hydrochloride on the market.

#### THE EFFECT OF HEAT OF EMETINE HYDROCHLORIDE.

If the alkaloids of ipecac obtained during the assay process are allowed to remain on the steam bath after the ethereal solvent has evaporated, darkening and disintegration of the alkloids results. Of three experiments in which the alkaloids were kept at water-bath temperature for five minutes after the ethereal solvent had evaporated, 6.7 per cent., 6.0 per cent. and 3.0 per cent., respectively, of the total amount of alkaloids present was lost.<sup>1</sup>

Since the alkaloids of ipecac are somewhat sensitive to heat, and as emetine is one of the alkaloids of ipecac, attention was given to the influence of the heat used in sterilizing ampule solutions of emetine hydrochloride.

Experiments were made by selecting three different lots of U. S. P. emetine hydrochloric, assaying them volumetrically, weighing out the theoretical quantities based on the assays, to prepare definite volumes of solutions containing 0.5 Gm. anhydrous emetine hydrochloride per 100 mils; 0.5 grain anhydrous emetine hydrochloride per mil, and 0.666 grain anhydrous emetine hydrochloride per mil, respectively. These three solutions were placed in ampules, sealed and heated at about 115° C. until sterile. A very slight darkening of the solution occurred in each case. The three solutions were then assayed volumetrically with the following results, respectively:

0.512 Gm. anhydrous emetine hydrochloride,

0.485 grain " " "

0.687 " " " "

<sup>1</sup> Éwe, G. E., and Vanderkleed, Chas. E., Proceedings Penna. Pharm. Assoc., 1914, p. 275.

Therefore, it was concluded that ampule solutions of emetine hydrochloride do not materially alter in strength upon sterilization even if the heat employed is sufficient to cause a slight darkening of the solution.

Crystallized emetine hydrochloride was also tested for its resistance to the influence of the degree of heat ordinarily employed in sterilization.

A specimen of U. S. P. emetine hydrochloride was divided into three portions; these three portions were heated to 120° C., 100° C. and 80° C., respectively, until they ceased to lose weight, and were then assayed volumetrically with the following results:

Temperature of Heating.	Per Cent. of Anhydrous Emetine Hydrochlorids.
120° C.....	95.83
100° C.....	99.60
80° C.....	100.02

Therefore, it was concluded that crystallized emetine hydrochloride practically withstands ordinary sterilization temperatures.

#### THE EFFECT OF LIGHT ON EMETINE HYDROCHLORIDE.

The U. S. P. directs that emetine hydrochloride be protected from light.

Solutions of emetine hydrochloride also require to be protected from light. Experiments showed that diffused sunlight for a matter of weeks is required to just appreciably darken solutions of emetine hydrochloride and direct sunlight for at least three hours' duration is required to just appreciably darken solutions.

#### THE ACIDITY OF EMETINE HYDROCHLORIDE.

The hypodermic use of solutions of emetine hydrochloride is frequently attended with irritation at the site of injection. One of the possible factors contributing to the irritation is acidity of the emetine hydrochloride. Some processes for the manufacture of emetine hydrochloride finally yield the salt in a condition in which free hydrochloric acid is present. If this free hydrochloric acid is not carefully eliminated it will contribute to the irritation attendant upon injection.

The U. S. P. recognizes this possibility and requires that emetine hydrochloride in aqueous solution (1 in 20) be only slightly acid to



litmus. Emetine hydrochloride will readily retain 1 per cent. or more of free hydrochloric acid and not show its presence by appearance or odor. This excessively acid product will, of course, be only "slightly acid to litmus." Actual titration of a solution of emetine hydrochloride with a standard alkali solution in the presence of methyl red as indicator and a limiting of the free acid to a few tenths of a per cent., calculated as absolute HCl, are to be preferred over the present U. S. P. method of simply testing a solution with litmus.

In connection with the subject of local irritation attendant upon injection of emetine hydrochloride solution, it may be of interest to mention that experiments on human subjects indicated that less local irritation was experienced when the solutions were prepared with distilled water than when prepared with normal saline solution. This was ascribed to the fact that the solutions made with distilled water were more closely isotonic with the blood.

#### THE EFFECT OF TIN ON SOLUTIONS OF EMETINE HYDROCHLORIDE.

A specimen of emetine hydrochloride, answering all of the U. S. P. requirements and having an acidity to methyl red equivalent to less than 0.1 per cent. absolute HCl was dissolved in distilled water to make a 2 per cent. solution. Tin foil, assaying 99.83 per cent. metallic tin, and containing traces of lead, iron and aluminum was allowed to stand in contact with the solution of emetine hydrochloride at room temperature for two weeks. At the end of this time the solution contained a considerable quantity of a whitish flocculent precipitate, the tin being apparently unaffected. This whitish flocculent precipitate when centrifuged out and washed with water was practically entirely soluble in ether. The ether solution yielded a substance upon evaporation which gave reactions for the alkaloid. A control experiment without tin remained perfectly clear.

Another specimen of emetine hydrochloride, answering all of the U. S. P. requirements and having an acidity to methyl red equivalent to less than 0.1 per cent. absolute HCl was dissolved in distilled water to make a 2 per cent. solution. Some of the tin foil used in the previous experiment was placed in the solution and the solution was then heated on a water bath under a reflux condenser for one day. A small quantity of precipitate like that yielded by the previous experiment was obtained. The conclusion is that

metallic tin acts similarly to a soluble alkali in liberating alkaloid from solutions of emetine hydrochloride, the time required, however, being prolonged.

ANALYTICAL LABORATORY OF THE  
H. K. MULFORD COMPANY.

SAPO MOLLIS U. S. P. IX.

BY BERTHA MUELLER,

ASST. PHARMACIST AT THE LANKENAU HOSPITAL, PHILADELPHIA.

Opportunity has recently been afforded us to try out the U. S. P. formula for *sapo mollis*, and we have found that the formula is satisfactory, though the technic is not. Indeed, it is quite inconceivable just why the technic should be so unnecessarily cumbersome and unpractical, when it must be conceded that it is an exceedingly simple matter to make soap.

According to the pharmacopœia, one is directed to dissolve the potassium hydroxide in a capacious vessel by means of heat, add the cotton seed oil, stir actively for a few moments, reapply the heat until the mixture froths due to boiling, add the alcohol, stir some more, and then stop in the midst of it to assay the preparation! It is only natural that the question should arise: Why all this extra work? Certainly just as good a soap can be prepared by a far more simple method.

It is common knowledge that artificial heat is not actually necessary in the manufacture of soap, and certainly not where alcohol enters into the combination. It is likewise a well-known fact that alcohol is rapidly vaporized in the presence of a high degree of temperature, therefore the small amount of alcohol in the given formula must perforce be largely driven off when added, as directed, to a boiling hot mixture in a capacious vessel; consequently the object of putting alcohol into soap in order to increase its detergent power is defeated.

It has been our experience, if the caustic potash solution is sufficiently concentrated and a suitable vessel be used, that soft soap can most easily be made without the aid of heat and with very little expenditure of time and labor.

The potash should be dissolved in an equal weight of water and

in a container that will retain the heat developed during the process of solution. It is well that the container should not be any larger than is necessary to hold the finished product, and if possible, it should be a deep vessel in preference to a shallow one. When solution has taken place, the oil should be added, followed by the alcohol. The mixture should then be stirred with occasional intermittance until saponification has taken place, which takes from 15–20 minutes, and can be readily recognized by the mixture assuming the nature of a thick smooth paste, the color of which gradually becomes clearer on stirring. At this stage the rest of the water may be added with possibly an occasional stirring until it is all absorbed and a clear soap results.

That one should have to stop in the midst of the process in order to carry out an assay, is most troublesome and equally unnecessary, for the pharmacopœia directs that the percentage strength of the potash should be known before hand and the amount of oil required should be calculated accordingly. Now, if one is tolerably careful in weighing out these materials, how can there be any doubt of the proper outcome with regard to alkalinity?

It may perhaps be pertinent to suggest that framers of formulas give more consideration to simplicity in technic in order that pharmacists may be encouraged to do more of their own manufacturing, by which means a more intimate knowledge of our official text books would be gained and with it the interest in them stimulated. Incidentally pharmacists would get a great deal of satisfaction and pleasure out of doing just such work, for there is truly much in pharmacy that is highly interesting.

## IODOGLYCEROLE.

BY E. S. TALBOT, M.D.

CHICAGO, ILL.

This preparation was first used in the treatment of so-called pyorrhea alveolaris in 1878 and for the general cleaning of the gums and mucous membranes before operating and has been continuously in use in my practice since that date.

It was found that when the official tincture of iodine was used that it removed the mucous membrane of the mouth. It was also



soon evident that different strengths of iodine were required with different patients. Likewise, that a more astringent preparation was necessary. After much experimenting the following formula was produced and is commonly known as

TALBOT'S IODOGLYCEROLE.

Zinc iodide .....	15 parts.
Iodine .....	25 parts.
Distilled water .....	10 parts.
Glycerin .....	50 parts.

This preparation can be diluted with water to suit any mucous surface. The formula has been extensively used in dental practice throughout the world.

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THE FEDERAL BOARD FOR VOCATIONAL EDUCATION  
WANTS EVERY DISABLED SOLDIER AND  
SAILOR TO KNOW—

That the government is resolved to do its best to restore him to health, strength, and self-supporting activity.

That until his discharge from hospital care the medical and surgical treatment necessary to restore him to health and strength is under the jurisdiction of the military or naval authorities.

That the vocational training which may be afterwards necessary to restore his self-supporting activity is under the jurisdiction of the Federal Board for Vocational Education.

That if he needs an artificial limb or other orthopedic or mechanical appliance the Bureau of War-Risk Insurance supplies it free upon his discharge and renews it when considered necessary.

That if, after his discharge, he again needs medical treatment on account of his disability the Bureau of War-Risk Insurance supplies it free.

That any man whose disability entitles him to compensation under the War-Risk Insurance Act may be provided by the Federal Board with a course of vocational training for a new occupation.

That the government strongly recommends each man who needs it to undertake vocational training and put himself under the care of the Federal Board, but the decision to do so is optional with each man.

That if his disability does prevent him from returning to employment without training and he elects to follow a course of vocational training provided by the Federal Board, the course will be furnished free of cost, and he will also be paid as long as the training lasts a monthly compensation equal to the sum to which he is entitled under the War-Risk Insurance Act or a sum equal to the pay of his last month of active service, whichever is the greater, but in no case will a single man or a man required by his course of instruction to live apart from his dependents receive less than \$65 per month, exclusive of the sum paid dependents; nor will a man living with his dependent receive less than \$75 per month, inclusive of sum paid to dependents.

That if his disability does not prevent him from returning to employment without training and he elects to follow a course of vocational training provided by the Federal Board, the course will be furnished free of cost to him, and the compensation provided by the War-Risk Insurance Act will be paid to him, but no allowance will be paid to his family.

That in addition to the above the family or dependents of each disabled man will receive from the government during his period of training the same monthly allotment and allowance as that paid prior to his discharge from the Army or the Navy.

That upon completion of his course of training he will continue to receive the compensation prescribed by the War-Risk Insurance Act so long as his disability continues.

That in nearly every case, by following the advice and suggestions of the Federal Board, he can either get rid of the handicap caused by his disability or acquire new powers to replace any that may have been lost.

That if he is willing to learn and to take advantage of the opportunities to increase his skill offered him by the Federal Board he can usually get a better position than he had before entering the service.

That if he fails to take advantage of these opportunities he will find himself badly handicapped when he is obliged to compete with the able-bodied men who come back to work after the war.

That the Federal Board, through its vocational experts, will study his particular disability and advise him as to the proper course to pursue and give him free training for the occupation best suited to him.

That on the satisfactory completion of his training the Federal Board, through its employment service, will assist him to secure a position.

That public authorities and other large employers will in many cases, at least, give the disabled soldiers and sailors preference when filling vacant positions, provided they possess the training necessary to fill them.

All disabled soldiers, whether in or out of the hospital, should address their communications either to the Federal Board for Vocational Education, Washington, D. C., or to the district office of the Federal Board of the district in which he is located. The district offices of the board are located at the following points respectively:

District No. 1: Maine, New Hampshire, Vermont, Massachusetts, and Rhode Island. Office: Room 433, Tremont Building, Boston, Mass.

District No. 2: Connecticut, New York, and New Jersey. Office: Room 711, 280 Broadway, New York.

District No. 3: Pennsylvania and Delaware. Office: 1000 Penn Square Building, Philadelphia, Pa.

District No. 4: District of Columbia, Maryland, Virginia, and West Virginia. Office: 606 F Street N.W., Washington, D. C.

District No. 5: North Carolina, South Carolina, Georgia, Florida, and Tennessee. Office: Room 1404 Candler Building, Atlanta, Ga.

District No. 6: Alabama, Mississippi, and Louisiana. Office: 822 Maison Blanche Annex, New Orleans, La.

District No. 7: Ohio, Indiana, and Kentucky. Office: 906 Mercantile Library Building, Cincinnati, Ohio.

District No. 8: Michigan, Illinois, and Wisconsin. Office: 1600 the Westminister, 110 South Dearborn Street, Chicago, Ill.

District No. 9: Iowa, Nebraska, Kansas, and Missouri. Office: 517 Chemical Building, St. Louis, Mo.

District No. 10: Minnesota, North Dakota, and South Dakota. Office: Room 742 Metropolitan Bank Building, Minneapolis, Minn.

District No. 11: Wyoming, Colorado, New Mexico, and Utah. Office: 909 Seventeenth Street, Denver, Colo.

District No. 12: California, Nevada, and Arizona. Office: 997 Monadnock Building, San Francisco, Calif.

District No. 13: Montana, Idaho, Oregon, and Washington. Office: Room 539 Central Building, Seattle, Wash.



District No. 14: Arkansas, Oklahoma, and Texas. Office: 810 Western Indemnity Building, 1000 Main Street, Dallas Texas.

*Editorial Comment.*—It appears to us that pharmacy opens up to many of these returning disabled soldiers and sailors an exceedingly inviting field for future professional careers and unusual possibilities for them to make, likewise, notable commercial successes. The schools of pharmacy are anxious to coöperate with the Federal Board for Vocational Education and the Philadelphia College of Pharmacy some time since placed before the officials of District No. 3, the facilities of the college and the desire of its officers and faculty to aid in every way possible in the education of such returning men of the service who desired to secure an education in pharmacy or chemistry.

## WAR CHEMISTRY AND MEDICINE.<sup>1</sup>

The signing of the armistice and the prospect of a long, if not permanent, peace have lifted the veil of secrecy that has long hidden many undertakings of great scientific interest in connection with the war. Only a few months ago every one was saving fruit kernels and nut shells at the behest of the American Red Cross. It was vaguely known that the materials were to be converted into charcoal, which was to be employed in the manufacture of gas masks. But why these particular products were selected, what became of them, and how they act were questions that belonged to the great mass of mysteries developed by the secrecy of war time.

Colonel Burrell,<sup>2</sup> chief of the research division of the chemical warfare service, has at length disclosed some of the "inside history" of his service. The absorbent value of charcoal of a suitable sort is extraordinary. During its preparation, a film of hydrocarbons is likely to remain adherent to the surface of the particles. To remove this is highly important, because it seriously diminishes the absorptive power. American initiative, guided by chemical science, found a way to overcome the difficulty. By oxidizing processes the charcoal was cleansed of its hydrocarbon film and rendered active.

The extraordinary and utterly unexpected diversity of gases and

<sup>1</sup> Reprinted from *Jour. Amer. Medical Assn.*, March, 1919.

<sup>2</sup> Burrell, G. A., "The Research Division, Chemical Warfare Service," *U. S. A., J. Indust. and Engin. Chem.*, 11, 93, 1919.

other noxious substances employed by our enemies in their warfare<sup>3</sup> early taxed the ingenuity of all the Allies to devise satisfactory respirators. At first an alkaline solution was sufficient to protect against inhalation of chlorin; but when phosgene, prussic acid, xylol bromide, chlorpicrin, bromacetone and a succession of other equally formidable products had to be taken into account, cheesecloth impregnated with alkali or even with sodium phenate and hexamthylenamine no longer saved the wearer of the mask from untoward effects. The soda-lime finally developed and used in masks contained lime, cement, infusorial earth, sodium hydroxide, sodium permanganate and water. Each ingredient performed a definite function. The lime furnished the main part of the absorption for acid gases, which it neutralizes, generally with the formation of calcium chloride. The cement is used to make the granules sufficiently hard and yet not decrease the porosity, which is fatal to good absorption. Several other binders give equally good hardness, but all destroy the porosity. The infusorial earth is used to increase the porosity of the granules and thus permit the gas to have access to the interior and utilize the full absorptive capacity of the granule. The sodium hydroxide activates the rate of absorption of most gases, and, in addition, makes the control of the drying process more simple and tends to maintain the proper water content in the finished granule. The sodium permanganate is used primarily to oxidize certain oxidizable gases, which are difficult to absorb in gas masks. The water is necessary in making up a satisfactory mixture, and, after drying, a fairly definite moisture content is needed to get the best results in the absorption of gases.

Nor is the story of prophylactic measures against chemical modes of warfare completed with the description of the gas masks. Since most of the casualties from the widely used mustard gas were due to skin burns, it became necessary to devise suitable protective clothing. Gummed suits might be appropriate in winter, but they became a physiologic impossibility in hot days. Yet even this handicap was finally overcome by the designing of suits that were not impermeable to air and moisture, yet absorbed mustard gas vapor.

Some day an orderly account of the almost infinite variety of chemical problems that the government was called on to answer in this war will be written. It will be a story of fascinating interest.

<sup>3</sup> "War Gases and Chemical Warfare," editorial, *J. A. M. A.*, 71, 1742, (November 23), 1918.

We shall learn how one scientist devoted his energies to the production of metal Dewar flasks for providing liquid oxygen to aviators; how another one spent days in finding the best way to disperse toxic solids or liquids, producing a fine powder or mist to penetrate masks; how many others worked unceasingly to synthesize new types of toxic compounds of arsenic or selenium or tellurium, whereupon colleagues tested their pharmacologic potency; how face masks with nondimming eyepieces were made comfortable for working and sleeping hours; how helium was extracted from natural gas to replace hydrogen in balloons. Now that the war is over we can pause to consider innumerable scientific advantages of the ceaseless labor and investigation of the past months. The thought that went into the war work, says a reviewer of its details, cannot be destroyed. The industries have gained much through the personal sacrifices of American chemists; likewise has medicine. The charcoal, the gas mask, the many potent new compounds, the liquid oxygen, the protective clothing, the dispersoids—these and dozens of other discoveries will surely find an application, somehow, somewhere, some day.

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## MODERN PAINT VEHICLES.<sup>1</sup>

BY JAMES E. HECKEL,

CHIEF CHEMIST, JOHN LUCAS & CO., INC.

During the four years just past, the German lust for world dominion, now happily rendered impotent, at least for a century or two, succeeded in disturbing greatly many of the normal customs, channels of supply and sources of information, of the sane portion of the world's population.

Gradually, as the need for tonnage to supply our forces and carry them "over there" increased, the pressure on us at home increased. We were forced by a long and complex chain of circumstances to meet a shortage of all sorts of materials which everyday habit had taught us to regard as essential and in the same class with air and water. Many familiar substances enlisted or were drafted, and right

<sup>1</sup> A paper read before the annual convention of the Pennsylvania Master House Painters' and Decorators' Association. Reprinted from *Drugs, Oils and Paints*, February, 1919.



in the middle of the winter of "nineteen hundred-and-freeze-to-death," as it was called, both coal and food went to war.

To all of us who were connected with the paint and varnish trades, one of the most serious of these shortages was that of linseed oil.

We were so accustomed to having sufficient linseed oil for our requirements, that the shortage in ships and the consequent government embargo on the importation of flaxseed from the Argentine Republic, brought us up quite suddenly with a cold chill at our closeness to a very serious shortage in our linseed oil supply.

The annual production of American flax has been insufficient and decreasing for the last decade and very noticeably so during the last two or three years. We had been getting into the habit of depending more and more on the Argentine and of late years on Canada, to help us make good our demand and the requirements of consumers of paint.

The normal annual consumption of flaxseed in this country is between 25,000,000 and 30,000,000 bushels; while our annual production for some years past has been well under 20,000,000 bushels, so you see we are far from self-supporting. For the first part of 1919 the government has lifted the embargo on Argentine flax and authorized the importation of some 3,000,000 bushels. This, of course, will help some, but the problem will never be solved, at least in peace times, by trying to satisfy the industry with a percentage of its absolute needs. A "drop in the bucket" is still a "drop in the bucket," even if the drop be extra large and the bucket only a thimble.

-In normal times there are just three means of overcoming the shortage: increase flax production; import enough seed to make up the shortage; or use other oils to eke out.

The first method of solution has been the aim of the Flax Development Committee and the Educational Bureau of the Paint Manufacturers' Association. The work of this committee, started in 1907, when conditions were very acute during that year because of the failure of the crop, cannot be too highly praised. To quote from the circular of the Bureau: "No more effective work has ever been accomplished (not even by the German Government) in behalf of any industry than this work for the paint industry of the United States. The committee has wisely contented itself with selecting

the men who understood the subject and supplying them with the necessary funds for educational work among the flax growers."

Incidentally, it is just such intelligent coöperation as this that has placed the United States far ahead of all other nations in the scientific and modern development of its painting and decorating industries. The presence of some of us here today is another evidence of that close and friendly coöperation, which like intelligent competition, is the "life of trade."

Before the Flax Development Committee began its work, the belief was prevalent among the farmers of the Northwest that soil on which flax had once been grown could not again be used for this purpose. There was some cause for this belief because the disease known as "flax wilt" was very destructive and the crop did impoverish the soil. The committee chairman, however, through the agricultural experiment stations, showed the farmers that flax could be grown on the same soil every fourth year in proper rotation with certain other suitable crops. This was a most valuable work and has and will recover a large acreage for flax.

The greatest difficulty lies in the price of wheat, averaging 31 bushels for each acre, fixed by the government at \$2.26; so that the farmers do not see much in flax averaging 10 bushels per acre, at \$3.00 or even \$4.00 per bushel.

The second means of relief was, as we have seen, practically cut off by the shortage of ships.

The third, the line of least resistance, was taken by the largest purchaser of paints, the United States Government.

It is then with a discussion of the possible substitutes for linseed oil, that the War Service Committee of the Paint Manufacturers' Association and the government experts were most highly concerned.

After many meetings and much discussion, the several departments of the government issued, during the last year or two, a number of specifications permitting the use of relatively large percentages of soya bean oil or refined fish oil at the option of the manufacturer. Certain other well known oils would have been equally acceptable if they could have been obtained in quantity. Among these may be mentioned lumbang ("Kukui" or candlenut oil), perilla and hemp-seed oils.

If the "life of a paint is good oil," so much more is the life of the liquid or vehicle portion of that paint "good oil." The question

resolves itself into "What is good oil?" and finally "What is a paint oil, and when is an oil a paint oil?"

In general, when we speak of a paint "vehicle," we mean all the liquid portion of the paint.

This vehicle can, in all cases, be split into two fairly distinct parts: the "volatile oils or thinners" and the "non-volatile or fixed oils," which form the bulk of the vehicle.

Among the "volatiles" (which can be distilled off from the rest of the paint in a current of steam and examined separately) we include turpentine (both wood turpentine and gum spirits), the various turpentine substitutes and benzine or naphtha.

The only comparatively new materials here are the turpentine substitutes, which possess many valuable properties, and which for the last ten or fifteen years have been distilled from petroleum either of asphaltic or paraffine bases. They are bought and sold under very rigid requirements and specifications as regards flash point, distillation, specific gravity, etc.

By far the largest part of the vehicle consists of the non-volatile or fixed oil portion. This usually consists of pure linseed oil, except in the flat wall paints and the enamels, which in one case may contain China wood oil, and in the other contain varnishes.

The non-volatile or fixed oils fall naturally into two great classes: (1) vegetable and (2) animal oils and fats. These two groups are both further sub-divided by chemists into four sub-groups: (1) solid fats; (2) non-drying oils; (3) semi-drying oils; (4) drying oils.

The solid fats are not of interest to us. The non-drying oils (even when vegetable or animal, and not mineral), are not of interest either to the conscientious manufacturer or master painter. The last class (the drying oils) and sometimes a mixture of one or more of them with a properly balanced percentage of one of the third class of semi-drying oils, is the only group which is really worth our attention. Drying oils suitable for use in paint may be either vegetable (linseed, soya, perilla) or animal (fish or menhaden) oils. Experiments and tests have even been made on whale oil and porpoise jaw oil, to indicate the breadth and scope of the field of investigation, but they were not very satisfactory.

The next questions which naturally come to mind at this point are: "How does a drying oil dry?" and "Why does it dry to an elastic film, while some other oils do not; and some (the heavy mineral oils) never dry?"



The complete answer to these questions is very complex, but the differences in behavior are inherent in the chemical structure of the individual oils. Nature has failed to complete the so-called drying oils, leaving them unbalanced (or as the chemists put it, "unsatisfied"), while the drying oils are complete chemical combinations with their chemical "affinities" satisfied. The drying oils are therefore ready to take on additional atoms to make a complete or satisfied compound. When hydrogen is added, as in the hydrogenation process, we obtain a fixed oil or fat (often edible), and when oxygen is added, as in the ordinary process of "drying," we obtain the familiar paint or varnish film.

The absorption of oxygen by linseed and other drying oils is progressive and continues long after the oil would be called "hard dry" by the painter, although very slowly. The dried film of linseed oil is known as linoxyn and contains about 16 per cent. by weight of oxygen which has been added in the drying process, plus, of course, the oxygen originally in the oil's composition. This increase in weight occurs in all drying oils, when they are exposed to the air (which consists one fifth of oxygen); and in some is greater than others.

The fats, waxes and the non-drying oils cannot absorb oxygen because they are "satisfied" compounds to start with; while the name of the semi-drying oils explains their position as intermediate between the drying and the non-drying oils.

In order to determine the relative values of various drying oils we have to determine the percentage of oxygen which they will absorb, the greater the oxygen absorption, the higher the siccative or drying power of the oil.

Now it is absolutely impracticable to add gaseous oxygen directly to a liquid oil and get it to combine in a way that can be measured. This difficulty has been solved by dissolving the oil in chloroform and adding a known excess quantity of iodine dissolved in acetic acid to the oil. The oil acts upon the iodine and combines with it, just as it does with oxygen, but much more rapidly.

After a definite length of time, the chemist determines how much iodine is free; that is to say, has not combined with the oil; the difference between this and the total quantity of iodine brought in contact with the oil represents the quantity added to or absorbed by the oil.

This so-called "iodine number" or "iodine value," therefore,

serves, within limitations, as a measure of the relative serviceability of oils for use in paints. It is expressed in terms of per cent. by weight of iodine absorbed; an iodine number of 185 therefore signifies that the oil will absorb 185 per cent., or almost twice its own weight of iodine.

Paint and oil chemists become so familiar with the relative iodine values that an oil is instinctively classified, at least to some extent, as slow or quick drying, as soon as its iodine number is given.

These iodine numbers will vary slightly, even for the same oil, depending on when the seed was gathered, where it was grown, etc., at least in the case of linseed and soya bean oils.

The iodine values of the various drying oils, with the highest given first, range in order roughly as follows:

Oil.	Iodine Number.
Perilla .....	190-212
Linseed .....	175-200
Menhaden fish .....	155-175
China wood .....	150-170
Candlenut or Lumbang .....	135-165
Poppyseed .....	135-145
Soya bean .....	120-140

These represent pretty nearly the extreme variation, although I have seen a sample of lumbang oil, probably impure, which showed the extremely low iodine number of 115.

The half hundred odd samples of linseed oil, representing shipments received in 1918 by John Lucas & Co., ranged from 182.3 minimum to 185 maximum iodine value. Since the specifications of the American Society for Testing Materials require that pure raw linseed oil from North American seed shall show a minimum iodine value of not less than 180, all of the above shipments represented pure raw linseed oil, as far as could be told from a determination of the iodine value.

During the same period, the samples of soya bean all ranged from 132.1-136.9, indicating very good quality oil also, since prime soya oil, of paint making quality, should show an iodine number of about 133. One sample of perilla oil showed an iodine number of 190.4 and a sample of lumbang 162.8. Properly refined menhaden oil shows an iodine value closely approximating linseed oil. These figures are given as indicative only, but they serve to show that all of these oils have, to some extent at least, one of the properties that makes linseed oil valuable.

There are several other chemical, as well as physical characteristics of drying oils, which are very important for their proper valuation. Among these we may mention acid number or value, saponification value, specific gravity and index of refraction.

The acid number is a measure of the free fatty acids present in an oil. It is always small in quantity, but very injurious when excessive, tending, as experiments indicate, to cause livering and hardening of paints in the can.

The maximum acid number permitted for raw linseed oil in prepared paints when pure is six.

Acid numbers of samples of various oils will vary roughly as follows:

Perilla .....	8-12
Linseed .....	2- 4
Menhadden .....	6.8
Soya bean .....	2- 4
Lumbang .....	1- 9

One sample of perilla oil which came to my attention showed an acid number of 11.2. The very high acid value of perilla oil, contrary to expectations, does not seem to cause any harm. Perhaps research would show the free acids in perilla oil to be of different composition than those of linseed. However that may be, paints made from perilla oil remain soft in the can, while paints made from linseed oil of equally high acid number would harden and "liver" in less than six months.

The soya bean oil samples analyzed varied from 2.05 to 3.70 in acid number. The impure sample of lumbang oil showed the ridiculous acid number of 52.0. Of course, no one would attempt to use oil of this sort. Whenever a very high acid number is found in an oil, the presence of rosin is at once suspected; and there is a test, the well-known Liebermann-Storch reaction, by which its presence or absence may be fairly well confirmed.

The specific gravity and the other so-called "constants" of oils are very helpful in identifying them when pure, but when mixtures are obtained, the task becomes exceedingly difficult.

Some of the vehicles used in paints made on government specifications are exceedingly complex, and contain various types of China wood oil, rosin and other varnishes. The results obtained in the application of literally thousands of gallons of paints containing all



sorts of ultra-modern vehicles, to all sorts of surfaces, are being observed with much interest by their designers.

We are now prepared to give some sort of answer to the question, "Why linseed oil?" First: because it is accessible, easily obtainable and entirely familiar. Painters know more about it than they know about any other oil. We are most of us mentally lazy and content to let well enough alone. There may be something just as good as even better, but why worry after the ideal when the real adequately serves?

Gentlemen, the war has jammed us out of that state of mind. Progress is not made by people contented to let well enough alone. That mental habit is responsible for the present-day condition in China. The man who is not continually seeking for something better is of no more use to civilization than a dog chasing his own tail. If we cannot lead, we should be willing to follow the leaders or at least give them a respectful hearing.

Today occasional shipments of perilla oil are being offered at a price just a little higher than linseed, usually—and from what is even now known about perilla oil, many men would just as willingly have perilla as linseed oil paint.

A progressive man in this industry cannot for a moment subscribe to the conclusion that it is the business of the manufacturer to give the painter what he wants, with all the complication that goes with that advice. On the contrary, the manufacturer has generally led in the progress of the industry and has forced his discoveries into practice. For example, when colors in oil were first offered in this country by John W. Masury, he found it almost impossible to persuade the painters of his day to use them.

With regard to some of the promising fields for soya oil, we may quote circular No. 50 of the Educational Bureau of the Paint Manufacturers' Association entitled "Soya Oil in Paints," and written by H. A. Gardner, director of the scientific section, whom you all know. He says: "For many years the makers of high-grade prepared paints have used pure linseed oil as a liquid for such paints, adding the usual small amount of drier and thinner required to form a practicable paint suitable for immediate use. Whenever rosin oil, gloss oils, or neutral petroleum base oils have been used as such, partially or wholly, to replace linseed oil in such paints, disastrous results may follow. There is, however, a class of pure vegetable oils produced from seed in the same manner as linseed oil, which have a

thoroughly legitimate use in the paint industry. Of these oils, soya bean oil is the most prominent. From the standpoint of resistance to exposure it compares favorably with linseed oil. One of the most promising uses for soya oil is for the grinding of oil colors. When used for this purpose, soft pastes are produced which do not become hard even upon long standing (probably because of the very low acid value of soya bean oil). Moreover, the amount of soya oil that would be introduced into a white paint base as a result of the use of such colors would be extremely small, since relatively small amounts of color are required for making most tints or shades."

This brings us once more to the question of the newer paint oils. What shall or can the painter do with them? Speaking broadly, I should say—nothing! Proper laboratory facilities and expensive tests, lasting over many months, and sometimes years, are necessary to prevent endless complaint and trouble from the use of the wrong material for the wrong job.

Soya bean oil, properly freed from moisture, by mild heating, may be an exception to this rule. So far as tests have indicated, twenty-five per cent. of such oil added to a good grade of linseed performs in all respects like straight linseed oil.

Of hemp oil we know very little in this country, but European experience and its chemical and physical characteristics warrant the expectation that when made available, it will make an acceptable substitute.

Perilla oil has worked out very nicely for varnish, besides being a first-class paint oil. Typical rosin, China wood oil varnishes containing perilla oil, showed slightly better wearing qualities when exposed to weather than those made with linseed oil.

Lumbang oil is also a varnish oil, but with proper treatment may be useful in paints.

The *Philippine Journal of Science* for September, 1917, contains a most interesting article on the "Comparison of Linseed Oil and Lumbang Oils as Paint Vehicles," by R. H. Aguilar.

He describes tests and gives results of analyses on two varieties of lumbang oil, lumbang bato and lumbang banucalag. The oils are expressed from the seeds of trees, lumbang bato coming from the candlenut tree, which is known in Hawaii as kukui. This tree is very widely distributed through India and Malaya to the Islands of the Pacific.

The other variety of the lumbang comes only from the Philippine Islands.

Aguilar, after a long series of tests, comes to the conclusion that the drying properties of both the lumbang oils are comparable to those of linseed; that the bato oil, in particular, is very similar in paint-making properties to linseed, but like linseed has certain disadvantages for use with red lead.

He finds that the banucalag variety cannot be used as a paint vehicle and dries into a paste with red lead. (The explanation may be partly in its high acid value of 8.70, while the bato variety showed an acid value of only 1.05.)

A very interesting oil for red lead was found in a mixture of banucalag containing between 50 and 75 per cent. bato oil. This gives a paint which does not harden, like paint made from linseed or either of the lumbang oils alone. It is also claimed that the various "painting out" properties of the resulting paint, are better than that of one made from linseed oil alone!

Sunflower seed oil did not turn out as promising for paint use as was first expected.

Properly refined fish or menhaden oil (the "odorless" variety!) appears to have met all physical requirements except that it has a tendency to darken—in other words, it is not apparently satisfactory for use with whites and tints, but it has been used largely in outside green cantonment paint for the U. S. Army, and on rigid specifications as to purity.

Many other oils, such as llalementia and chia, are under investigation, both from an agricultural and technical point of view, but nothing very definite can be said of them as yet.

With respect to chia oil, a gentleman who had been in Mexico before conditions became so satisfying to lovers of Bolsheviki conditions of living, exported chia nuts to this country for over two years. The oil from these was used by someone who may have been a little more progressive or better equipped than the rest of us, who it was I do not know.

The discussion would not be complete without some mention of the various "dope" oils, near linseed oils and other patent remedies for the ailments of the trade which are so widely advertised.

Some of these are most excellent for the purposes intended, and are sold absolutely on their own merits as substitute oils, not "equal



to linseed." Other sellers are not so conscientious and sell with the intention of defrauding the public.

A practical drying test on glass, and a comparison of the resulting time of drying, nature of film formed, etc., will often give a good idea of the relative value of these oils compared to linseed oil.

Some samples of this type of material would not dry, but remained tacky for over 144 hours. Others gave hard, brittle films containing rosin.

The net result of the foregoing hasty summary is that unless the painter is equipped to investigate or is willing to trust the paint manufacturer who is equipped both to investigate and to produce, he had better make the best of what he knows—pure linseed oil—as long as he can obtain it.

We all remember how in "Through the Looking Glass" a person had to run just as fast as he could to stay right where he was. If you wanted to get ahead, it was necessary to put on a wonderful burst of speed. So it is with this, and all other modern industries; much of our time is occupied keeping up to the times, so let us not be too confident that there is not a wider art or a deeper science than our own. Such confidence may entail a rude awakening.

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## BENZYL ALCOHOL.<sup>1</sup>

BY LECTURER ON PHARMACY,  
UNIVERSITY OF SYDNEY.

Benzyl alcohol is the latest addition to our list of local anæsthetics, and one likely to prove of great value. In these days of cocaine shortage and restriction it will be particularly welcome.

As a chemical compound we have known benzyl alcohol for about a century, and its constitution has been thoroughly established. It belongs to the aromatic series of carbon compounds, and is isomeric with the three cresols having the molecular formula  $C_7H_8O$ . It differs from the cresols in constitution, the hydroxyl group occurring in the side chain ( $C_6H_5CH_2OH$ ); it is also known as phenyl carbinol, and may be considered as methyl alcohol, in which one hydrogen atom of the methyl group is replaced by phenyl. Its alcohol char-

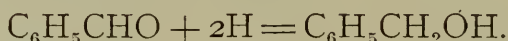
<sup>1</sup> Reprinted from *The Chemist and Druggist of Australasia*, January, 1919.

acter is already indicated by this formula. The cresols are phenols, the hydroxyl group being attached to the carbon ring  $C_6H_4OHCH_3$ .

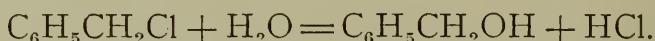
Benzyl alcohol is a derivative of toluene  $C_6H_5CH_3$ , one hydroxyl group replacing hydrogen in the methyl group. When oxidized it follows the general reaction for primary alcohols, being converted into an aldehyde (benzaldehyde  $C_6H_5CHO$ ) and on further oxidation into an acid (benzoic acid  $C_6H_5COOH$ ).

It occurs naturally free, and combined with anisic and benzoic acid in certain resins, storax, balsam of Tolu and balsam of Peru.

When benzaldehyde is reduced by nascent hydrogen (sodium amalgam) benzyl alcohol is produced.



It is also formed when benzyl chloride is boiled with a solution of sodium carbonate; hydrolysis takes place, and the hydrochloric acid set free is neutralized by the carbonate.



#### PREPARATION.

A very convenient and practical way of preparing pure benzyl alcohol is by means of potassium hydroxide on benzaldehyde.



It will be seen from the equation that two molecules of benzaldehyde are required to produce one molecule of the alcohol, in other words 212 Gm. of benzaldehyde will theoretically yield 108 Gm. of alcohol, and by the practical method given below 90 per cent. of this theoretical yield may be obtained. If necessary the benzoic acid can be recovered from the potassium benzoate.

Dissolve 90 Gm. of solid potassium hydroxide in 60 mls. of water, cool to air temperature ( $15^{\circ} C.$ ) and transfer to a 500–600 mil. stoppered bottle, add 100 Gm. benzaldehyde, and shake well until a permanent emulsion is formed.

Allow to stand until the following day (15–20 hours), during which time the mixture solidifies owing to the separation of a mass of white crystals—potassium benzoate. Water is added with shaking until all the crystals have dissolved.

The mixture is next agitated with ether to remove the benzyl alcohol. Allow the ethereal layer to separate; repeat the extraction three or four times.

The mixed ethereal layers are washed with a small quantity of saturated solution of sodium bisulphite to remove any unchanged benzaldehyde. Separate the ether, and filter. The filtrate, which consists of a solution of benzyl alcohol and ether is evaporated (the ether may be recovered by distilling). The residual oil is almost entirely benzyl alcohol, and is fractionated by distillation. At first a little ether may be obtained; this is rejected, the greater part passes over between 204–207° C., and consists of pure benzyl alcohol.

Although usually stated in text books to be only very slightly soluble in water, it is dissolved to the extent of 4 per cent. The boiling point of benzyl alcohol is 206° C., therefore much higher than water. It is not decomposed at the temperature of boiling water, hence it may be sterilized at that temperature.

*The Medical Journal of Australia*, August 3, 1918, reports that "this new anæsthetic has been tested in the surgical clinic of Professor W. Halstead and elsewhere. A report of fifty cases dealing with the incision of abscesses, the excision of toe nails, the extraction of bullet from the hand . . . has demonstrated the efficiency of 1 per cent. aqueous solution as an anæsthetic."

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## THE PREPARATION OF ARSPHENAMINE (SALVARSAN).<sup>1</sup>

BY PHILIP ADOLPH KÖBER.

I. INTRODUCTION.—The synthesis of an arsphenamine or salvarsan suitable for therapeutic purposes, in spite of the work of Ehrlich and Bertheim<sup>2</sup> and their collaborators, is still a vital problem. It is fairly well known that the toxicity of arsphenamine varies and that batches made by individual manufacturers vary more than can be accounted for by the differences in their procedures. Furthermore, since it seems fairly well proven that even Ehrlich's own manufacturers are unable to maintain a uniformly high standard,<sup>3</sup> it is evident that there are some factors which are not understood or not under control. I am informed by manufacturers of

<sup>1</sup> Read in part before the Society of Experimental Biology and Medicine, New York City, November 20, 1918. Reprinted from *The Journal of the American Chemical Society*, March, 1919.

<sup>2</sup> *Ber.*, 45, 756, 1912.

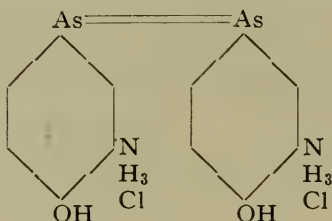
<sup>3</sup> Roth, *Hygienic Laboratory Bulletin* 113, 7, 1918.



arsphenamine that about 50 per cent. of the arsphenamine made does not meet the Surgeon General's requirements<sup>4</sup> and therefore is not distributed.

In studying the subject, I came to the conclusion that the toxicity of arsphenamine or at least the variation of the toxicity is largely due to the use of methyl alcohol and ether in the final precipitation of the base as the dihydrochloride. While most chemists use Ehrlich and Bertheim's methyl alcohol and ether method or some modification of it for precipitating the dihydrochloride of salvarsan, not one will admit, or is willing to believe, that the dry product contains a molecule of methyl alcohol.

The theoretical amount of arsenic in arsphenamine as shown by the formula is 34.2 per cent., assuming that it is absolutely pure and contains no water or solvent in its crystal or solid form.



The German firm having a monopoly of the manufacture of the drug, tried at first to get the scientific public to accept its statement unchallenged of a 34 per cent. arsenic content. Analyses by others soon compelled them to abandon that claim and for seven years 31.6 per cent. (31.57 per cent.) has been and now is accepted as the arsenic content.

This different and smaller content of arsenic is in harmony with an assumption of two "molecules of water of crystallization" in the final dry substance.

This amount of water is given in the literature frequently and by the U. S. Health Service regulations<sup>5</sup> as an actual fact, and a higher content of arsenic, involving less solvent combined with the drug, is looked upon with suspicion.

I believe I have exhausted the references to the literature on this point, and I can find no justification for assuming two molecules of water in the drug, made by the usual and original directions.

<sup>4</sup> The U. S. Public Health Service, *P. H. Reports*, 33, 540, 1918, requires an M.L.D. of 0.060 g./kilo body weight, while the Surgeon General (recently) raised the requirement to 0.080 g./kilo, and to 0.100 g./kilo.

<sup>5</sup> *Public Health Reports*, 33, 540, 1004, 1918.

The reference or work chiefly if not wholly relied upon for this assumption is that of Gaebel.<sup>6</sup> Myer<sup>7</sup> and DuMez quote him also in support of the arsenic regulations of the drug. While other authors make arsenic estimations, Gaebel is the only author mentioned or that I can find, beside Ehrlich and Berthéim, who has made any experiments as to the solvent and its amount in the dry substance.

Gaebel passed hydrogen gas, purified, over 0.07966 Gm. salvarsan, contained in a glass-vessel called "Ente" (meaning goose-shaped), heated in an oven at 105° C.; the vapor coming off was tested only for hydrochloric acid with silver nitrate solutions. He weighed the "Ente" and noted the loss of weight. After 6 hrs. its weight became constant and the loss corresponded to 7.2 per cent. The theoretical loss for 2 molecules of water would be 7.6 per cent.

This one estimation apparently satisfied him for he records no duplicate estimation, and called the solvent thus lost water, apparently taking no account of the fact that arsphenamine was actually precipitated from methyl alcohol (undoubtedly anhydrous so as to mix with the ether) with non-aqueous ether. That Gaebel simply assumed it to be water, not knowing the method of Ehrlich and Berthéim used is indicated also by the fact that he published a year before Ehrlich and Berthéim published their method.

Against the statement that the solvent in the solid arsphenamine is water, are the words and experiments of Ehrlich and Berthéim.<sup>8</sup> They tested one preparation made with methyl alcohol and ether, in the same way all their preparations are supposed to be made, after drying the substance at 65° C. in a current of carbon dioxide. This temperature is about the boiling point of methyl alcohol. On dissolving this dried preparation in water and distilling over any volatile solvents they found methyl alcohol in appreciable quantities. They concluded upon this and other reliable analyses that it contained one molecule of methyl alcohol for every molecule of the arsphenamine.

In view of these facts, it seems fairly certain that arsphenamine made according to the original directions must contain methyl alcohol, unless, of course, it is removed by drying under more favorable conditions than Ehrlich and Berthéim used. The evidence in the literature gives one the strong impression that for commercial reasons its methyl alcohol content has been kept secret. The ob-

<sup>6</sup> *Apoth. Ztg.*, 26, 215-216, 1911.

<sup>7</sup> *Public Health Reports*, 33, 1004, 1918.

<sup>8</sup> *Ber.*, 45, 756, 1912.

jections to methyl alcohol and other considerations connected therewith will be discussed on page —. In order to eliminate the methyl alcohol or any other organic solvents in the process of preparation, the following method was developed:

II. METHOD OF PREPARATION.—Finding that the dihydrochloride of the arsphenamine base was insoluble in an excess of chlorides, as might be expected from the Law of Mass Action,<sup>9</sup> an excess of hydrochloric acid was tried in "salting" out the drug. When first tried, by making an aqueous solution of the dihydrochloride directly from the base, by dissolving in twice normal sodium hydroxide and adding a slight excess of hydrochloric acid and then pouring the solution of hydrochloride into a strong solution of hydrochloric acid (1-1), a white precipitate was formed which, however, soon turned to a dark-colored gum. This transformation of the white precipitate into the black gum, was due simply to the coalescence of the particles. This coalescence was prevented when the precipitation was conducted, (1) at a low temperature, (2) under more dilute conditions, and (3) with vigorous stirring.

As the purity of the hydrochloride depends also on the purity of the arsphenamine base, the details of this preparation will be briefly given; in other words, the process starting with the nitro-oxyphenyl-arsonic acid<sup>10</sup> will be described.

1. *Reduction of Nitro-Oxyphenyl-Arsonic Acid*.—Two hundred and twenty (220) grams of magnesium chloride are dissolved in 5,500 Cc. of distilled water and 1,100 grams of sodium hydrosulphite are quickly added, while stirring or shaking, in an eight-liter bottle.

To this solution is then added, with stirring or shaking, 85 grams of crude nitro-oxyphenyl-arsonic acid, dissolved in 290 Cc. of 2.0 *N* sodium hydroxide and diluted with 1,700 Cc. of water. The mixture<sup>11</sup> is then allowed to stand at room temperature or it is slowly

<sup>9</sup> Nernst, *Z. phys. Chem.*, 4, 372, 1889; Noyes, *ibid.*, 6, 241, 1890.

<sup>10</sup> Owing to the ease with which *p*-arsanillic acid can now be made, which is described in a separate communication (*Journal of the American Chemical Society*, 41, 300, 1919), we prefer to make nitro-oxyphenyl-arsenic acid by nitrating the oxalic acid derivative of *p*-arsanillic acid (*Ber.*, 44, 3095, 1911) and saponifying according to the directions of Ehrlich and his collaborators (*Ber.*, 44, 3451, 1911).

<sup>11</sup> These amounts of material and solution practically fill an eight-liter bottle, so that little, if any, inert gas is needed nor do other anaërobic precautions have to be taken.



warmed in a water bath at 40° C., until the suspension, first formed, seems to agglutinate and to be about to settle. The suspension matter seems to be impurities, mostly dark colored, from the nitro-oxyphenyl-arsonic acid; impurities from the hydrosulphite, also dark, and its reaction products; besides a little of the arsphenamine base. The total weight of the suspension, when filtered and dried, is rarely more than three to four grams, or four to five per cent. of the total yield.

When this stage is reached, the mixture is rapidly filtered, through hard paper, or alundum ware, and the clear, yellow filtrate digested, according to Ehrlich and Berthelm's directions, at 50° to 60° C. for two to two and a half hours, when the base—diamino-dioxyarsenobenzene — separates out as a yellow precipitate.

Some chemists lay great stress on using only the purest nitro-oxyphenyl-arsonic acid and only to treat it subsequently with commercial hydro-sulphite, which itself, in many cases gives, if not a muddy solution, at least a dark colored one; all this in spite of Ehrlich and Berthelm pointing out, that the reduction, even with the purest nitro-oxyphenyl-arsonic acid, produces its own by-products. These chemists then rely on bone-black to remove all such impurities from the hydrochloride in methyl-alcohol solution.

This preliminary digestion of ours and filtering removes the impurities to such an extent, that with the exception of a slight white, mineral

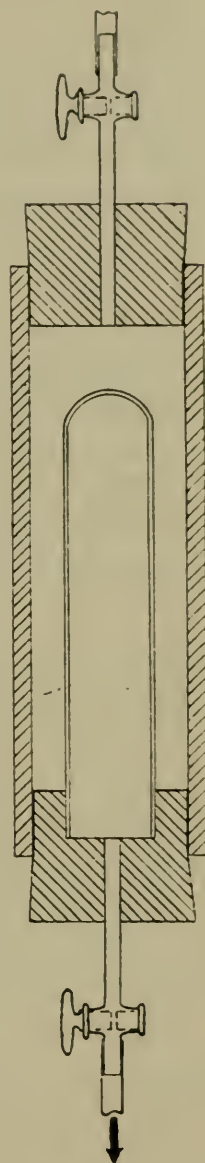


FIG. 1.

Laboratory Anaerobic Filter.

The outer cylinder may be made of glass, and the inner cone of "alundum" ware. When not completely filled with liquid, inert gas such as hydrogen or nitrogen is introduced and the position of the filter reversed.

residue found in some hydrosulphites, no further filtering or removal of extraneous coloring matter is necessary.

2. *Preparation of the Dihydrochloride.*—The crude diaminodioxarsenobenzene, after filtering and washing with distilled water at  $0^{\circ}$  C., is transferred to a porcelain dish and suspended in 400 Cc. of distilled water, likewise at  $0^{\circ}$  C., where it is dissolved in the least quantity of two normal sodium hydroxide, usually about 150 Cc., which should be at  $0^{\circ}$  C. We find it convenient to prepare all the necessary solutions two or three days ahead of time and to keep them in an ice-box or refrigerator, at the end of which time they will be cold enough for the purpose.

The alkaline solution of the base is now filtered so as to remove any insoluble matter, like filter paper; any fibers of dust, and also, a small amount of the mineral precipitate, mentioned before, which is present when some hydrosulphites are used. For this purpose we have constructed a simple form of anaërobic filter, which is shown in Fig. 1.

To the perfectly clear alkaline solution of the arsphenamine, 150 Cc. of strong hydrochloric acid (1-1) at  $0^{\circ}$  C. are added, which throws out and re-dissolves the yellow base. The clear solution, resulting from the addition of the hydrochloric acid, contains the dihydrochloride, and, for the purpose of getting a fine precipitate, the solution is further diluted with distilled water at  $0^{\circ}$  C. in order to bring the volume of the final solution up to 1,700 Cc.

Into a stirring apparatus, 3,250 Cc. of hydrochloric (acid 1-1, *i. e.*, 1 part concentrated acid plus 1 part water) at  $0^{\circ}$  C. are placed. While vigorously stirring, the cold aqueous solution of dihydrochloride of arsphenamine is run slowly into this hydrochloric acid. The grey-white precipitate, now formed, is allowed to settle for an hour. It is then filtered in thin layers and dried in a vacuum desiccator at a low pressure, fused calcium chloride and solid sodium hydroxide in sticks or flakes<sup>12</sup> being used as absorbents. It is preferable to place the solid alkali separately in a dish surrounded by the calcium chloride. The heat of neutralization of the hydrochloric acid, undoubtedly, helps to a considerable degree to dry the substance quickly. After twelve or more hours hydrogen is introduced into the desiccator to equalize the pressure and the

<sup>12</sup> Flakes, containing 97 per cent. of sodium hydroxide can now be obtained for about 6 cents a pound.

arsphenamine is ground and further dried until of constant weight. The yield is about 75 per cent.

III. THE PRODUCT.—*Color*.—The substance prepared by the method just described is usually a greyish powder sometimes having a slight yellowish tint. When very pure it seems to have little or no color and is practically white in a dry state, and is possibly analogous to the color changes of cupric sulphate when made anhydrous.

*Analysis*.—Analyses of preparations having about 1 molecule of water in the final product are as follows:

Preparation.	Per Cent. As. <sup>13</sup>		Per Cent. N.		Per Cent. Cl.	
	Found.	Theory.	Found.	Theory.	Found.	Theory.
No. 2 .....	32.67	32.85	...	...	...	...
No. 5 .....	...	...	...	...	14.89	15.50
No. 12 .....	32.89	32.85	6.37	6.13	14.09	15.50

Preparations with 2 molecules of water in the final product gave:

Preparation.	Per Cent. As. <sup>13</sup>		Per Cent. N.		Per Cent. Cl.	
	Found.	Theory.	Found.	Theory.	Found.	Theory.
No. 9 .....	31.83	31.57	5.60	5.90	16.79	14.90
No. 10 .....	31.83	31.57	5.64	5.90	14.09	14.90
No. 11 .....	30.38	31.57	5.83	5.90	14.67	14.90

The analyses that Ehrlich and Bertheim obtained on their product are given below for the purpose of comparison. One analysis made by us of arsenobenzene is also given. The theoretical values are calculated on the basis of 1 molecule of methyl alcohol to 1 molecule of arsphenamine.

Preparation.	Per Cent. As.		Per Cent. N		Per Cent. Cl.	
	Found.	Theory.	Found.	Theory.	Found.	Theory.
Ehrlich and Bertheim's ...	31.99	31.85	6.06	5.95	14.51	15.07
Arsenobenzol No. 1449 ...	30.89	31.85	6.20	5.95	15.24	15.07

<sup>13</sup> The above results are in most cases the averages of the following analyses. The arsenic estimations were made according to the gravimetric method described in Treadwell-Hall (1914) and also in *Public Health Reports*, 33, 1003-1018, 1918. The nitrogen was determined according to the Kjeldahl method (modified Gunning), U. S. Department of Agriculture, *Bull.* 107, 8d, 1907. The chlorine was determined by fusing the product with two parts of potassium nitrate and one part of sodium carbonate and then proceeding according to Drechsel modification of Volhard's method. Treadwell-Hall, 2, 707, 1914.



Ehrlich and Bertheim found that in the same preparation just mentioned the carbon content was 32.63 per cent. The theory for 1 molecule of methyl alcohol calls for 33.12 per cent. C., while the theory for 2 molecules of water requires only 30.32 per cent. C.

*Qualitative Tests.*—Of the qualitative tests suggested and compiled by Meyer<sup>14</sup> and DuMez, we have tried the following ones only, which we consider the most important, and obtained the reactions described in every respect:

*Dilute sulphuric acid* gave an insoluble hydrosulphate.

*Nitric acid* gave the characteristic color.

Preparation.	Per Cent. As.	Per Cent. N.	Per Cent. Cl.	Per Cent. Sulphur.
No. 9. ....	32.01	...	...	
	31.86	...	...	
	31.62	...	...	
	31.95	...	...	
	31.21	5.60	16.84	
	32.32	5.67	16.75	
Average .....	31.83	5.63	16.79	
No. 10 .....	31.02	...	...	
	31.62	...	...	
	32.11	...	...	
	32.34	...	...	
	31.77	5.64	14.18	
	32.11	5.64	14.00	
Average .....	31.83	5.64	14.09	
No. 11 .....	30.43	...	...	
	30.90	...	...	
	30.25	5.78	14.72	
	29.93	5.88	14.63	
Average .....	30.38	5.83	14.67	0.30
No. 12 .....	32.62	...	...	
	33.07	...	...	
	33.00	...	...	
	33.07	6.30	14.18	
	32.71	6.45	14.00	
Average .....	32.89	6.37	14.09	

*Bromine water* gave the color described.

*Phosphotungstic acid* gave the color reaction for phenols.

*Silver nitrate* gave the beautiful red colored complex described by Danysz.<sup>15</sup>

<sup>14</sup> *Public Health Reports*, 33, 1004, 1918.

<sup>15</sup> *Compt. rend.*, 157, 644, 1913; *ibid.*, 158, 199, 1914.

*Magnesium mixture*, used as described, showed no inorganic arsenic.

*Mayer's reagent for alkaloids*, gave the characteristic test.

*Mercuric chloride* showed the precipitate described.

*Carbon dioxide* precipitates the base from its alkaline solution, as is very characteristic for salvarsan, showing the presence of a very weakly acid substance.

*Physical Properties*.—The substance as soon as it is moistened with water becomes brownish yellow and dissolves in 5 parts of water to form a gel or gelatinous solution depending on the temperature. It is readily soluble in warm or hot water, slightly soluble in methyl alcohol, scarcely soluble in ethyl alcohol, insoluble in ether or benzene.

*Melting Point*.—It does not melt slowly when heated, but gradually darkens, beginning at 160° C.; when at about 180° C. it begins to char. Ehrlich and Bertheim state that their product decomposes, depending on the speed of heating at about 185–195° C. with charring.

*Toxicity*.—In general its other properties seem to be that of salvarsan in every respect. When tested by injection into rats according to the rules and standards recommended by the U. S. Public Health Service and adopted by the Federal Trade Commission,<sup>15</sup> it seems to have a relatively low grade of toxicity.

IV. GENERAL DISCUSSION.—Our work on arsphenamine seems to show that the dihydrochloride, when pure and possessing only one or two molecules of water, is practically colorless. Samples of this colorless form can be shown and are easily prepared. Impure arsphenamine is tinted more or less, depending on the impurity and also on the physical form of the solid substance. Of the three commercial preparations made in America no two are alike in color. The Canadian Diarsenol is very yellow, the Metz preparation less yellow with a tint of green, while the Arsenobenzol has a light yellow tint.

The amount of yellow tint may be due to the sulphur content, as our gray substances have about one half to one fourth the amount of sulphur that is present in the ordinary yellow material.

The analyses of arsphenamine indicate that the amount of colored impurity in most preparations must be negligibly small, at most 1 per cent. or less. The toxicological studies also show that the

<sup>15</sup> *Public Health Reports*, 33, 540, 1918.

amount of colored impurities is small and negligible. In fact Ehrlich,<sup>17</sup> G. T. Morgan<sup>18</sup> and we in this laboratory have found that a very light-colored arsphenamine is sometimes very toxic compared to a darker preparation. Since it is possible also to alter the color of the solid form by changing its physical state, comparison of the color of different arsphenamines should be based on the color of the substance in standard solutions.

To sum up: The color of the solid arsphenamine seems to be due to a small amount of highly colored impurities in an otherwise colorless substance.

Our experience with the methyl alcohol and ether method has brought to our attention four possible objections against the use of these substances: These solvents are highly inflammable; they are expensive even in peace times; they are difficult to make pure, and finally methyl alcohol, ether and other solvents are easily oxidized to easily reducible substances. As a concomitant with arsphenamine, a substance easily oxidized to very toxic and therefore dangerous products, methyl alcohol and similar substances, are *a priori* not safe to use or have present.

The advantages of the hydrochloric acid method are:

(a) The medium of precipitation, both the water and the hydrochloric acid can be absorbed by common and inexpensive absorbents; they are not easily oxidized or reduced.

(b) It is an inexpensive method as the excess hydrochloric acid can be recovered ready for use by simple distillation.

(c) It requires no inflammable material.

(d) The reagents used are pharmacologically suitable and raise no question as to toxicity, such as does the use of methyl alcohol and ether.

(e) The product, being less hygroscopic, is less liable to oxidation and other chemical change, when exposed to the air, and is therefore more stable.

(f) The method, as some preliminary experiments show, can be used for reprecipitation, and from a chemical standpoint seems better calculated to eliminate impurities.

The same method is used to obtain sodium chloride of the highest purity for atomic weight work.

<sup>17</sup> *Loc. cit.*

<sup>18</sup> Longmans, "Organic Compounds of Arsenic and Antimony," 1918, p. 156.



My thanks are due to Mr. Leonard M. Wachter for making the special tests and for supervising the analytical work, and to Mr. F. W. Gilcreas for careful and painstaking analytical work.

V. SUMMARY.—(1) It is shown that there is no justification for Gaebel's assuming two molecules of "water of crystallization" in salvarsan made according to the directions of Ehrlich and Bertheim. While Gaebel made his assumption apparently in ignorance of Ehrlich's and Bertheim's method published a year later, no valid reason can be given for the general acceptance of that assumption since Ehrlich and Bertheim pointed out in 1912 that their preparation contained one molecule of methyl alcohol.

(2) A new method which is much less expensive and simpler than Ehrlich and Bertheim's method has been developed for the preparation of the dihydrochloride of arsphenamine base in pure aqueous solution by means of hydrochloric acid, being salted out similarly as in the precipitation and purification of sodium chloride with hydrochloric acid.

(3) The final product of the new method may have one or two molecules of water depending upon the drying. This seems to be the first time the dihydrochloride of the arsphenamine base has been prepared without organic or other solvents in combination or present in the final product.

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## FURTHER FACTS REGARDING ANTISCORBUTICS.<sup>1</sup>

Scurvy, a disease which once represented a menace of serious moment to large numbers of persons at certain seasons and under certain conditions, when "fresh" foods were not available in sufficient variety or abundance, has returned into prominence in recent years. Experience has shown that while the heating of milk for infant feeding may remove undesirable bacterial dangers from this essential food, it is liable at the same time to destroy certain undefined properties of the diet, in the absence of which scorbutic symptoms arise. Furthermore, under the conditions of food supply enforced in some of the theaters of war, the medical officers have also found themselves confronted with scurvy, both among the fighting units and among the inhabitants of devastated areas.

<sup>1</sup> Reprinted from the *Journal of the American Medical Association*, March 8, 1919.

Quite aside from all theories as to the etiology of the disease, experience has demonstrated effective methods for the cure or the prevention of scurvy. In this country orange juice has acquired a growing popularity as an antiscorbutic supplement to the diet of bottle-fed infants. The difficulties in maintaining a supply of oranges at a price within the reach of all classes of persons concerned have been aggravated by the interference with normal transportation during the period of the war. This has, in fact, occasioned much concern among pediatricians in various centers. The possibility of desiccating or preserving the juice in some way at the source of supply in order to insure a more dependable distribution of orange juice has encountered the obstacle of uncertainty raised by recent studies on the instability of antiscorbutic properties when vegetables exhibiting them are dried.<sup>2</sup> Thus the desiccation of cabbage seems to deprive it of antiscorbutic potency unless the drying is carried out at low temperatures and with special precautions. Chick and Rhodes,<sup>3</sup> of the Lister Institute for Preventive Medicine in London, have recently found, in searching for possible substitutes for the highly efficient orange juice, that fresh grapes are of little value as antiscorbutics; of the raw vegetable juices examined, raw swede juice proved to be far the most potent, approximating in value to orange juice; the raw juice of carrots was found to be much inferior, and that of beet roots practically negligible in value, so far as acceptable dosage is concerned.

From a practical standpoint the discovery of this potency of swede juice seems to be important because it promises to afford a valuable, inexpensive source of antiscorbutic material. According to the English investigators, the value of swede juice is not markedly inferior to that of fresh orange juice, so that it may be regarded as a satisfactory substitute. Its value approximates ten times that of the raw carrot and more than ten times that of the raw beet root juice. Chick and Rhodes add that swede juice has been adopted in some of the English infant welfare centers, and there does not appear to be any drawback to its use in infant feeding. Curiously enough the swede belongs to the natural order Cruciferae, which also

<sup>2</sup> "Scurvy and Antiscorbutics," editorial *J. A. M. A.*, 71, 2000 (December 14, 1918).

<sup>3</sup> Chick, Harriette, and Rhodes, Mabel, "An Investigation of the Antiscorbutic Value of the Raw Juices of Root Vegetables with a View to their Adoption as an Adjunct to the Dietary of Infants," *Lancet*, 2, 774 (December 7), 1918.

includes the cabbage, perhaps the most potent of all antiscorbutic vegetables investigated.

In the case of adults living under conditions in which fresh foods are not available, a belief in the antiscorbutic potency of the juice of the West Indian lime has been cherished for decades. Arctic explorers, ships starting on long voyages without access to land, and expeditions away from sources of appropriate food supplies have been accustomed to be equipped with lime juice preserved in various ways; and there are records to show that vigorous steps were sometimes taken to enforce the actual injection of the dosage as ordered. The efficacy of this preventative therapy has been far from universal; and an explanation seems to be afforded by recent investigations, also conducted at Lister Institute, by Chick<sup>4</sup> and her co-workers, to whom we are already indebted for valuable contributions to the prevention of scurvy. Preserved lime juice was found useless for the prevention of scurvy by the methods employed. The fresh limes have some potency; but it has now been shown that, volume for volume, their juice is only about one fourth as effective as is lemon juice. Curiously enough, a historical study of the reported cures of scurvy with lime juice shows that the agent employed in several authenticated cases was in reality the juice of the lemon. There are instances of severe scorbutic outbreaks despite the liberal use of lime juice. This demonstrated virtue of the lemon, a fruit so widely employed in the household in modern life, affords an added illustration of the unique value of many items of diet, like certain fruits and green vegetables, for which we pay a high price despite the fact that they give no equivalent return in calories. Instinctively, perhaps, we have come to include in our dietaries articles of food which have a high physiologic value that cannot be measured in the current term of food units.

<sup>4</sup> Chick, Harriette, Hume, E. Margaret, Skelton, Ruth F., and Smith, Alice H., "The Relative Content of Antiscorbutic Principle in Limes and Lemons, Together with Some New Facts and Some Old Observations Concerning the Value of 'Lime Juice' in the Prevention of Scurvy," *Lancet*, 2, 735 (November 30), 1918.



## CURRENT LITERATURE.

## SCIENTIFIC AND TECHNICAL ABSTRACTS.

✓STAINING DIPHtheria BACILLUS WITH TOLUIDINE BLUE MIXTURE.—The staining solution which Sutherland has used for eight years has the following composition: Toluidine blue, 0.1 Gm.; glacial acetic acid, 0.5 Cc.; distilled water, 100 Cc. The smears are made on slides and fixed with heat in the usual way. When large numbers of cultures have to be examined, it is the most convenient to make the smears in a series of ten or twelve at one time. A drop of the stain is placed on each film and a cover glass is then placed over the preparation. The excess of stain is removed by blotting each slide between two layers of blotting paper immediately before being examined. The first slide is ready for examination about one minute after the stain is applied, and the others are taken in rotation. The best results are obtained by using strong artificial light. When slides are stained in this way the polar granules of *B. diphtheriæ* are of a deep reddish purple, while the bodies of the bacilli appear faintly blue. Most of the organisms found in diphtheria swabs, including Hoffman's bacillus, are more faintly stained, so that *B. diphtheriæ* is readily detected when present only in small numbers. The stain may also be used in a similar manner for demonstrating the bacillus in smears made direct from the swabs, in which case the film should be allowed to stand in the stain for from two to three minutes before removing the excess. (From *Lancet*, London, February 8, 1919, through *Jour. Amer. Med. Asso.*, March 15, 1919.)

OPIUM ANALYSIS.—D. B. Dott. The author criticises and discusses the paper by Annett and Singh (*Analyst*, 1918, 43, 205), in which these writers contend that the B. P. method of morphine estimation in Indian opium gives low results, mainly owing to the presence of codeine exerting a solvent action on the morphine and preventing its precipitation by ammonia from a solution of the lime compound. The author contends that it is hardly correct to speak of precipitation by ammonia, the morphine being really precipitated, because the chlorine of the ammonium chloride combines with the calcium, and the morphinate of lime, being decomposed, causes the precipitation of the morphine in the saline solution in which it is

very slightly soluble. Whatever may be the solvent action of codeine on morphine in aqueous solution, assay conditions are different, in that sufficient ether is present to hold all the codeine in solution. Annett and Singh's procedure of shaking the lime solution with toluene before treating with ether and ammonium chloride was tried, using benzene in place of toluene, with the resulting production of a frothy emulsion which makes extraction troublesome. This emulsion probably contains a small quantity of a basic lime compound which is readily separated by filtration, but is greater in quantity and more impure than the trace which always forms when using the B. P. process, where benzene is not employed. On comparing the two precipitates (the B. P. and the benzene treated), the latter, although heavier, shows on ultimate titration no more, and it may be slightly less than the former, and it is concluded that there is no sufficient reason for altering the process in the direction suggested by Annett and Singh. (*Pharm. J.*, 1918, 101, 318, through *The Analyst*, February, 1919.)

ESTIMATION OF ALDOSES IN ALKALINE SOLUTION.—The method of H. Colin and O. Liévin depends on the fact that, under certain conditions, dextrose is oxidized quantitatively to gluconic acid by iodine in alkaline solution. The alkalinity must be sufficiently faint to eliminate risk of oxidizing the alcohol groups. The author uses a solution containing 35 Gm. of sodium phosphate and 50 Cc. of  $\frac{N}{10}$  sodium carbonate in a liter. To the solution to be analyzed at least three times as much  $\frac{N}{10}$  iodine are added as will suffice to oxidize the dextrose believed to be present, and then a volume of the alkali solution about double that of the  $\frac{N}{10}$  iodine. After an hour the mixture is made faintly acid with sulphuric acid, and the excess of iodine titrated with thiosulphate. Proteins, tannin, and coloring matters which may react with iodine must first be removed. Usually, careful treatment with the least possible excess of lead acetate will suffice to remove the interfering substances occurring in the inulin-bearing roots, tubers and the like, for the analysis of which the method was worked out. (*Bull. Soc. Chim.*, 1918, [IV], 23, 403-405; through *The Analyst*, February, 1919.)

IODIMETRIC ESTIMATION OF HYPOPHOSPHITES AND PHOSPHITES. The method proposed by Boyer and Bauzil is based on the fact that hypophosphorous acid is oxidized by iodine in acid solution to

phosphorous acid; the latter is not further oxidized in acid solution, but if an alkali (sodium hydrogen carbonate) is added the oxidation proceeds a stage further to phosphoric acid. *Hypophosphites*.—Ten Cc. of the solution containing 0.1 Gm. of the hypophosphite (hypophosphites which are insoluble in water may be dissolved in dilute sulphuric acid) are placed in a stoppered flask, and treated with 10 Cc. of 25 per cent. sulphuric acid and 30 Cc. of  $\frac{N}{10}$  iodine solution; the mixture is kept in a dark place for ten hours, and the excess of iodine is then titrated with  $\frac{N}{10}$  thiosulphate solution. Each Cc. of  $\frac{N}{10}$  iodine is equivalent to 0.00328 Gm. of hypophosphorous acid ( $H_3PO_2$ ). *Phosphites*.—Ten Cc. of the solution, containing about 0.1 Gm. of the salt, are treated with 10 Cc. of 5 per cent. sodium hydrogen carbonate solution and 20 Cc. of  $\frac{N}{10}$  iodine solution; after two hours, 10 Cc. of 10 per cent. acetic acid are added, and the excess of iodine is titrated. Each Cc. of  $\frac{N}{10}$  iodine is equivalent to 0.00407 Gm. phosphorous acid. The method may be applied to mixtures of the two salts. (*J. Pharm. Chim.*, 1918, 18, 321, 334; through *The Analyst*, February, 1919.)

CONSTITUENTS OF OIL OF CASSIA—II.—F. D. Dodge. The author has identified benzaldehyde and methyl salicylaldehyde in oil of cassia. Neither of these substances has previously been shown to be present. In collaboration with Sterndale, the author has previously shown (*J. Ind. and Eng. Chem.*, 1915, 7, 155) that oil of cassia contains salicylic aldehyde (0.1 to 0.2 per cent.) coumarin benzoic acid, salicylic acid, and a liquid acid of fruity odor, not further identified. In addition to the above named substances, it has long been known that oil of cassia consisted mainly (75 to 90 per cent.) of cinnamic aldehyde, and that cinnamyl acetate and methyl ortho-coumaric aldehyde were present, whilst it has been stated, but scarcely proved beyond doubt, that phenylpropyl acetate is or may be present. (*J. Ind. and Eng. Chem.*, 1918, 10, 1005–1006. Reprinted from *The Analyst*, March, 1919.)

ANTISEPTIC VALUE OF SOME ESSENTIAL OILS.—L. Cavel. For each essential oil the minimum quantity was determined which was found necessary to prevent all bacterial growth in ordinary neutralized meat broth plentifully sprinkled with water from a septic source. The inhibiting quantity of phenol under the same experimental conditions being 5.6 parts per 1,000, the author obtained the



following classification for the essential oils: Thyme 0.7 part per 1,000, marjoram 1.0, orange-peel oil 1.2, verbena 1.6, cassia 1.7, rose 1.8, clove 2.0, eucalyptus 2.25, mint 2.5, geranium (rose de France) 2.5, vetiver 2.7, bitter almond 2.8, gaultheria 3.0, geranium (Indian) 3.1, wintergreen 3.2, meadow-sweet 3.3, spike-lavender 3.5, aniseed-tree 3.7, iris 3.8, common cinnamon 4.0, wild thyme 4.0, birch 4.8, anis 4.2, mustard 4.2, rosemary 4.3, cumin 4.5, neroli 4.75, lavender 5, balm 5.2, ylang-ylang 5.6, juniper 6.0, sweet fennel 6.5, reseda 6.5, garlic 6.5, lemon 7.0, cajeput 7.2, sassafras 7.5, heliotrope 8.0, cedrate 8.4, turpentine 8.6, parsley 8.8, violet 9.0, camphor 10.0, angelica 10.0, patchouly 15.0. Seven months after inoculation the culture plates were still sterile when the above quantities were used. (Cf. *Analyst*, 1918, 43, 171. *Comptes rend.*, 1918, 166, 827-829; through *Inter. Rev. Sci. Prac. Agric.*, 1918, 10, 1151. Reprinted from *The Analyst*, March, 1919.)

## MEDICAL AND PHARMACEUTICAL NOTES.

✓**"LINSEED SERUM" FOR BURNS.**—The following *Linoscrum* is recommended by J. Bandaline and J. de Paliakoff as a dressing for burns. The serum must be applied fresh the same day as it is prepared, and should be combined with hot air douches.

Infusion of linseed (1.5 per cent.) .....	1,000 Gm.
Chloride of sodium .....	9 Gm.

Filter and sterilize. (*Union Pharm.*, 1918, 59, 284, September; through *The Prescriber*, February, 1919.)

✓**RHEUMATISM AND MOUTH-BREATHING.**—T. M. Allison holds that rheumatism is invariably connected with mouth-breathing, and that the curative treatment of that complaint is the employment of gargles in addition to salicylates. He recommends the following:

R Acid. carbol. liq. ....	5 iv
Aq. chloroformi .....	ad 5 viii

Ft. garg. Sig.—"Half a teaspoonful in a glass of water as a gargle night and morning."

*B. M. J.*, 1918, 2, 421, October 12; through *The Prescriber*, February, 1919.)

✓**SCABIES.**—G. Milian recommends the following ointment as more absorbable than sulphur ointment:

Potassium sulphide .....	50 Gm.
Water .....	250 Gm.

Dissolve and incorporate with

Soft paraffin .....	250 Gm.
Lanolin .....	250 Gm.

Afterwards add

Zinc oxide .....	5 Gm.
Liquid paraffin .....	200 Gm.

(*Paris méd.*, May 18, 1918; through *The Prescriber*, February, 1919.)

✓ CASTELLANI'S MIXTURE.—This preparation, reported on by Guerrero *et al.* as of value in the treatment of yaws, has the following formula:

℞ Antimon. tartarat .....	0.065 Gm.
Sod. salicylat. ....	0.65 Gm.
Potass. iodid. ....	4.00 Gm.
Sod. bicarb. ....	1.00 Gm.
Aquam .....	ad 30.00 Gm.

This quantity is given in one dose, diluted in 4 ounces (120 Cc.) of water, thrice daily, to adult natives, one third or less to children, and half doses to Europeans. Pharmaceutically the mixture is not elegant: it is cloudy and has a sediment of antimony oxide. This, however, disappears on dilution, or may be avoided by the addition to the formula of 8 Cc. of glycerin. Castellani's original article is abstracted in *The Prescriber*, 1916, p. 264. (*Philippine Jour. Science*, 1918, 13, 191, July; through *The Prescriber*, February, 1919.)

✓ DAKIN'S SOLUTION: A NEW FORMULA.—The accepted formula for Dakin's solution<sup>1</sup> consists of chlorinated lime, sodium carbonate, sodium bicarbonate and water. The lime is mixed with water and allowed to settle; the sodium salts are dissolved separately in another quantity of water and the solution added to the lime suspension; the precipitated calcium carbonate is allowed to settle, and the clear fluid siphoned off. Notwithstanding the fact that in this formula the chlorinated lime has first to be titrated to ascertain the percentage of available chlorine, and the quantity of sodium salts

<sup>1</sup> See *American Journal of Pharmacy*, 1917, Vol. 89, pp. 396 and 497.

adjusted according to this percentage. C. Pagel (*Bull. des Sc. Pharm.*, 1918, 25, 263, Sept.-Oct.) considers that this solution is too alkaline, and he recommends the following modification: Mix the required quantity of chlorinated lime with the water, and filter off the clear liquor. Dissolve the sodium carbonate separately in water, and mix the solutions. Filter off the precipitated calcium carbonate, wash, and treat the precipitate with hydrochloric acid to form a solution of calcium chloride. The solution of sodium hypochlorite is then exactly neutralized with the calcium chloride solution. The product, he says, contains 0.5 to 0.6 per cent. of active chlorine, and is very stable. It has given great satisfaction in the hospitals in which it has been used. (From *The Prescriber*, February, 1919.)

**PASTE FOR ULCERATED WOUNDS.**—With a view to supersede the old-fashioned occlusive dressing with strips of plaster in the treatment of ulcerated wounds (note syphilitic), Morlet (*Presse méd.*, September 12, 1918) has devised the following paste:

Balsam of Peru .....	15.0 to	20.0 Gm.
Bismuth subnitrate .....	15.0 to	20.0 Gm.
Fish glue .....		50.0 Gm.
Glycerin .....		50.0 Gm.
Water .....		100.0 Gm.

This paste is absorbent and porous, constituting a semi-occlusive dressing which, while tending to dry the wound, also allows any pus formed to pass out. The wound is first cleansed with alcohol and its margins loosened; a bandage impregnated with the hot paste is then applied, covering the wound, and the dressing allowed to remain for from twelve to fifteen days. Usually one or two dressings are required, rarely three. The patient may walk about during the course of the treatment, the act of locomotion having the effect of an actual massage of the wound. (From *The Prescriber*, February, 1919.)

**BENZYL ALCOHOL AS A LOCAL ANÆSTHETIC.**—The value of benzyl alcohol, phenmethylool, or methyl-hydroxybenzene,  $C_6H_5 \cdot CH_2 \cdot OH$ , is reported on by D. I. Macht (*Jour. Pharmacol. and Exper. Therap.*, 1918, II, 263, Apr.) who concludes that it possesses powerful local anæsthetic properties with a very low toxicity. He considers that these properties, together with the simple excretion of the drug by the organism and the ease with which solutions



may be sterilized, are strong reasons for its use in surgery. Benzyl alcohol is a liquid with a faint aromatic odor, slightly soluble in water (1:25), and miscible in alcohol or ether in all proportions. A 4 per cent. solution in water or in normal saline solution is practically non-irritant and non-toxic, and may be used in the same way as other local anæsthetics. Owing to the high boiling point of benzyl alcohol (over 200° C.), the aqueous solution may be sterilized by boiling without loss of strength. The absence of toxicity is due to the fact that it is metabolized in the organism and excreted in an innocuous form. The drug is inexpensive, and is certainly deserving of further trial. (From *The Prescriber*, February, 1919.)

✓ MARYLEBONE CREAM (J. P., 8/4/18).—Cremor Maryleboniensis, as given in the St. Marylebone General Dispensary Children's Pharmacopœia, 1913, is as follows:

Linseed oil .....	1 ounce.
Benzoic acid .....	½ grain.
Gluside (saccharin) .....	½ grain.
Oil of bitter almonds .....	1 minim.
Decoction of Irish moss .....	2 ounces.

*Dose*: Half to one teaspoonful to be added to each bottle of diluted milk. This preparation is recommended as a substitute for cream in infant feeding. (From *The Prescriber*, February, 1919.)

✓ PROFLAVINE OLEATE IN TREATMENT OF WOUNDS.—Berkeley and Bonney draw attention to the value of proflavine oleate in the treatment of certain war wounds, notably those in which an exceedingly tender raw surface of considerable extent exists, the dressing of which is productive of acute pain. Their method consists in either spreading a thick layer of the oleate ointment on a single thickness of white gauze and then applying it to the wound, or spreading the oleate direct on to the surface of the wound and then covering it with a single layer of gauze. This dressing does not need to be changed for several days, and, when it is removed, strips off the sensitive surface without any dragging or pain. It is equally applicable to any large flat-surfaced wounds, such as those left after wholesale excision of the thigh or buttock muscles and so forth. The authors suggest that after all operations in which a flat raw surface is necessarily left, the wound should, from the first, be dressed with proflavine oleate, in the manner described. (*British*

*Medical Journal*, London, February 8, 1919; through *Jour. Amer. Med. Asso.*, March 15, 1919.)

FLY KILLERS.—Boyé and Guyot describe extensive research on and means to abate the fly nuisance. The practical conclusions are that castor oil and arsenic are the best fly killers. Castor oil containing a little sugar attracts the flies and they die in and around it. Its action is enhanced by adding 20 drops of croton oil to 30 Gm. of the castor oil. The fly dies almost instantly, while the oil is not dangerous for man. The odor of sugar and the odor of decomposing milk, flesh, or blood, seem to attract flies most powerfully. (*Bulletin de l'Académie de Médecine*, Paris; through *Jour. Amer. Med. Assoc.*, March, 1919.)

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## ANNUAL MEETING OF THE PHILADELPHIA COLLEGE OF PHARMACY.

The annual meeting of the college was held on Monday afternoon, March 31, 1919.

In his annual report, President Howard B. French presented a review of the year's work of the college and some of the special problems of the management. The following is an abstract of this interesting address:

During the past year the college has been doing extraordinary work by serving the government in many ways. Many of its students and alumni and several members of the faculty entered the government service in the army, navy, marine corps or in civil positions. Some have paid the extreme sacrifice, and to their memory we give all honor. To those who have returned disabled it becomes our duty to aid in every possible way to put them in positions where they can earn a competent and comfortable livelihood.

It is fitting that a proper and lasting memorial should be created in honor of those of our number who have so nobly gone forth to the service of their country, and a tablet placed on the walls of the college would seem a suitable memorial.

The war conditions have reduced very considerably the number of students in attendance and the solving of other problems growing out of the war conditions has caused your board of trustees much anxiety.

The college was able to render assistance to the government in the training of naval hospital corpsmen. One hundred and fifty such naval students were assigned to it, and this class was known as the United States Naval Hospital Corpsmen Training School of the Philadelphia College of Pharmacy, and was under the command of Lt. W. T. Minnick (M.D.), U.S.N. The course was intensive and practical and lasted about three months. Universal commendation was given to all connected with this work for the competent manner in which the unusual situation was managed.

A second class of thirty selected students was sent to the college and are now undergoing the same careful training.

During the year a number of the members of the faculty co-operated in the important work of examining medical, chemical and pharmaceutical supplies for the U. S. Army Supply Depot in this city and thus saved the government material expense. It is but proper that recognition should be given Professors LaWall, Stroup, Sturmer and Cook for their active coöperation in this work.

The reports from the departments show that the instruction has been kept fully up to the standard of former years, and a number of the faculty have assumed advanced positions in their teachings.

Although the advanced classes have been smaller and the special students fewer in number this year, twenty-one students were enrolled in the technical chemical course. It is interesting to note that a Japanese student has been taking special instruction in the preparation of toilet articles. He has taken a comprehensive course of instruction in this line and will be able to make many commercial products. The facilities created for this particular work will establish a basis for further instruction in this direction.

The leave of absence granted the librarian last June to temporarily accept government service, has prevented the usual report. The librarian has given as much attention as possible to the care of the library so as to keep the department in a satisfactory condition.

The secretary reports that during the year there were elected 134 active members and 83 associate members. This unusual number elected was largely due to the extra efforts made by the Alumni Association. During the year five members have died: James L. Bispham, of Philadelphia, a member for 64 years; C. Halsey Bogert, of Philadelphia; Roy L. Clark, of Utah; James H. Allan, of Maryland, and J. Oscar Burge, of Tennessee.

In order to increase the facilities of your institution it has been



deemed wise to secure amendments to the charter so as to broaden its scope and to provide for all of the various branches taught in the college.

We cannot overlook the fact that we are approaching our hundredth anniversary. Some of the alumni have thought it prudent to create a sustaining fund, and have arranged to begin active work in that direction. Members of the board and other friends are using their efforts to create a building fund of sufficient size to erect new buildings upon a proper site when obtained. Great work is to be accomplished and every effort must be put forth for a successful conclusion.

Appreciation is expressed for the active coöperation and assistance rendered by the faculty during one of the most trying years that the college has ever experienced and also to the members of the board of trustees for their most earnest and active support.

#### ANNUAL REPORTS.

*Committee on Publication.*—A detailed report of the financial condition and of the circulation of the AMERICAN JOURNAL OF PHARMACY was presented, likewise an estimated budget for the year 1919-20. The circulation of the JOURNAL was very materially increased during the year and considerable more revenue was derived from advertisements.

*Editor's Report.*—The year that has elapsed since the last annual meeting of the college and the prior report of the editor has been marked by the occurrence of epochal making events that must ultimately affect the readjustment of the social and economic status of the world as well as the political destinies of many nations. Pharmacy as one of the vocations directly associated with current events, in that it necessarily serves the present needs of the people, is bound to be influenced in its trade and practices by the existing unrest. It becomes thus a part of the duty of pharmaceutical journalism to influence as greatly as is possible the events affecting pharmacists and the drug trade so that the demoralizing effects of governmental errors and popular misunderstandings may be minimized.

The sense of this responsibility has impelled your editor to discuss current events relating to pharmacy in the editorial columns. In thus deviating from what had become almost a traditional policy of the JOURNAL, his judgment based upon an earnest internal deliberation on the subject, was that the AMERICAN JOURNAL OF

PHARMACY as a leading exponent of ethical pharmacy, could not refrain from giving proper consideration to important subjects and events influencing in any manner the services that pharmacists rendered to society.

The aim has been to maintain the AMERICAN JOURNAL OF PHARMACY as a true "Record of the Progress of Pharmacy and the Allied Sciences." That this has met with the approval of our contributors is evidenced by the list of the authors in the Index to the ninetieth volume. Despite the war conditions, the material available for publication necessitated the printing last year of 913 pages exclusive of the advertising. The varied character of the articles and subjects considered in that volume for 1918 is attested by the numerous titles in the index. It is believed that the JOURNAL is more extensively read than ever and it is noteworthy that many of our articles are republished or abstracted in other journals.

It is apparent that with the broadening of the scope of the JOURNAL that it is becoming less and less merely the medium of promulgating the actions of the college and is ceasing to be simply the journal of the Philadelphia College of Pharmacy, but that it is filling more faithfully, if possible, the sphere of an ethical pharmaceutical journal with an international reputation. It is believed that in performing this service professional pharmacy as a whole is benefited and that the college thus adds materially in advancing pharmacy and must indirectly in the end have not only that satisfaction that comes from altruistic service but likewise its due share in the reward.

The business management of the JOURNAL has rendered most efficient coöperation with the editor and the efforts to upbuild the circulation and the advertising patronage will doubtless eventually meet with the success merited. In the meantime, the joint work of the two departments will be continued and no pains will be spared to make the JOURNAL influential and progressive at a minimum of expense to the college. The report of the Publication Committee deals more specifically with this phase of the work.

Your editor is more concerned with the problems associated with making the JOURNAL of value and practical service to all branches of the drug trade and contributions, suggestions and constructive criticisms having that end in view are welcomed.

*Committee on Neurology.*—Reported deaths of members during the year as mentioned in the president's address, with concise memoirs and data of importance to the records of the college.

*Committee on Nominations.* Reported a list of nominees to be voted for as officers and trustees.

On behalf of the estate of Professor Joseph Remington, Professor LaWall presented a large photograph album containing the portraits of many of his prominent pharmaceutical associates; also a number of pieces of apparatus used in the lectures of the late dean. The thanks of the college were tendered the donors.

On motion of Professor LaWall the suggestion of President French that a memorial tablet to "our boys" be placed on the walls of the college, was referred to the board of trustees for action.

Mr. George M. Beringer, chairman of the board of trustees, presented amendments to the charter that were deemed necessary in view of the many advances made in the college work since the charter was amended in 1878. These amendments, four in number, were thoroughly discussed, acted upon, and severally adopted, as follows:

1. That the title of the college be changed from the "Philadelphia College" to "Philadelphia College of Pharmacy and Applied Sciences."

2. "That all restrictions as to the amount of income from any estate of the college be removed."

3. "That courses comparative to those given by universities and colleges in their scientific departments and by schools of applied sciences be instituted, and that degrees be awarded to our graduates from such courses agreeing with those awarded by such educational institutions for equivalent courses, and honorary degrees in pharmacy and in the sciences upon those meriting such distinction."

4. "That the number of trustees be increased from eighteen to twenty-four."

The officers of the college and the solicitors were empowered to take the necessary steps to secure these amendments to the charter.

*Election of Officers, Trustees and Committees.*—A ballot was taken and the following officers and committees were elected:

*President*—Howard B. French.

*1st Vice-President*—R. V. Mattison, M.D.

*2d Vice-President*—Joseph L. Lemberger.

*Treasurer*—Warren H. Poley.

*Corresponding Secretary*—A. W. Miller, M.D.

*Recording Secretary*—C. A. Weidemann, M.D.

*Curator*—Heber W. Youngken.



*Editor*—George M. Beringer.

*Librarian*—Katharine H. Nagle.

*Trustees Elected for Three Years*.—Samuel P. Sadtler, Wm. L. Cliffe, H. K. Mulford.

*Publication Committee*.—Joseph W. England, Chas. H. LaWall, Geo. M. Beringer, John K. Thum, J. W. Sturmer, R. P. Fischelis, E. F. Cook.

*Committee of Pharmaceutical Meetings*.—C. B. Lowe, M.D., Geo. M. Beringer, Chas. H. LaWall, E. Fullerton Cook, John K. Thum.

The following appointments were made by the president:

*Committee on By-Laws*.—George M. Beringer, Joseph W. England, C. A. Weidemann, M.D.

*Delegates to the Pennsylvania Pharmaceutical Association*.—Charles H. LaWall, chairman, Freeman P. Stroup, F. X. Moerk, E. Fullerton Cook, J. W. Sturmer, O. W. Osterland, John K. Thum.

*Delegates to the New Jersey Pharmaceutical Association*.—George M. Beringer, chairman, C. B. Lowe, Charles H. LaWall, J. W. Sturmer, H. W. Youngken.

*Delegates to the Delaware Pharmaceutical Association*.—A. W. Miller, chairman, C. B. Lowe, H. J. Watson, S. L. Foster.

C. A. WEIDEMANN, M.D.,  
*Recording Secretary.*

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## BOOK REVIEWS.

CHEMISTRY IN OLD PHILADELPHIA. By Edgar F. Smith, University of Pennsylvania. Printed by the J. B. Lippincott Company, Philadelphia, Pa., 1919.

In this small book of 106 pages the facile pen of Provost Smith has presented a very interesting and instructive story. The author, one of America's leading chemists and educators, demonstrates anew that the true scientist and student loves to delve into the historical mines of science and learns much from studying the characters, life works and services of those who, in the past, were devotees of the sciences in which he is now working.

The book presents in a most inviting manner the status of the knowledge of chemistry and physics and of some of the theories prevailing, in the colonial days and in the early period of the exist-

ence of the American Republic. Even in those early times, Philadelphia appears, as later, to have been the center of scientific learning in the western hemisphere, and the early chemists of the City of Brotherly Love were renowned as leading and influential citizens who made their impress upon scientific progress as well as upon the political events of the time.

To a Philadelphian, Dr. de Normandie, is ascribed the honor of having written the first chemical paper to appear in print in this country. In 1769, the University of Pennsylvania instituted the first chair of chemistry in America and Dr. Benjamin Rush was the first professor of chemistry in this country.

The individual contributions of the early Philadelphia chemists in behalf of their chosen science is necessarily presented in rather a cursory manner. A brief recapitulation, such as is permissible as within the scope of a review, may not be amiss.

Dr. Benjamin Rush, a leader in medicine. His greatest service possibly was in directing the attention of medical students to the value of cognate chemical studies.

Dr. Joseph Priestly, who emigrated from England in 1794 and thereafter established a permanent residence in Pennsylvania and whose influence in stimulating the study of chemistry at this time was paramount, encouraged a number of the Philadelphia scientific circle to apply themselves to experiment and chemical studies.

Thomas P. Smith, whose early contributions were full of promise and whose lifework was prematurely cut off at the age of twenty-five years.

James Woodhouse, who aided materially by his writings in the overthrow of the old doctrine of phlogiston and whose experimental work did much to establish true ideas concerning combustion, respiration and oxidation. His studies added much to our knowledge of the chemistry of plants. He also analyzed many minerals and it is stated first isolated the metal potassium.

Adam Seybert, renowned as a chemist and as a member of Congress from Philadelphia. He was a pioneer in air analysis and he, likewise, laid the foundation for physiological chemistry. In his later life he devoted his attention very largely to mineralogy.

His son, Henry Seybert also took up the study of minerals, "earnestly proceeded in his father's footsteps" for some years, until philanthropy, religiously observed, became almost his sole absorbing task.

Dr. John Redman Coxe, a noted medical practitioner, succeeded Dr. James Woodhouse as professor of chemistry in the University of Pennsylvania.

The disputative Thomas Cooper, a naturalized citizen of English birth and education, dabbling alike in politics, law and chemistry he served for a time as a district judge and as professor of chemistry in Dickinson College and later as the holder of the chair of chemistry and mineralogy in the University of Pennsylvania which he resigned and took up a professorship in a southern college.

Gerard Troost, a scholar said to have possessed a lovable personality; doctor of medicine and master of pharmacy by reason of education in European universities. He was noted for his profound knowledge and for his genius as an organizer and teacher. As one of the founders of the Academy of Natural Sciences of Philadelphia, he served as its first president and guiding spirit for a number of years. He was the first professor of chemistry in the Philadelphia College of Pharmacy. He specialized in the study of mineralogy and geology. In 1828, he left Philadelphia, to assume the professorship of chemistry in the University of Nashville and thereafter assiduously devoted himself to the study of his favorite branches. His published work in geology is considered authoritative and his life work is highly rated.

Professor William H. Keating, of the University of Pennsylvania, was another mineralogic chemist of high scientific attainment and interested greatly in the larger public affairs of his time.

Joseph Cloud smelter at the U. S. Mint whose work was largely concerned with the noble metals and the problems associated with the fusing points of metals and alloys.

The last name considered with the older chemists of Philadelphia is that of Professor Robert Hare. His contributions to chemical and physical sciences were not excelled by any of his predecessors mentioned and have scarcely been outclassed by any one whose name has yet been associated with the development of these branches of science. To him are we indebted for the compound blowpipe, the oxy-hydrogen flame, the first electric furnace, artificial graphite, calcium carbide, the mercury cathode and the rock blasting device. Many of these discoveries and inventions are even now in daily application in some of our most important industries.

The pen pictures of the author show that these men were not only influential in the development of chemistry but that they were



also factors in promoting other scientific and educational interests. The chemical societies of the time, the American Philosophical Society, the Academy of Natural Sciences, the Franklin Institute, etc., all reflected their activities as well as did the literature of the time which contained their published records of experiments and advances.

As we complete the perusal of this interesting contribution to the history of "Old Philadelphia" and the olden chemistry, we cannot refrain from expressing the wish that the author will continue his studies along these lines and write in the same fascinating style of the life works of the chemists who have worked in Philadelphia and vicinity in the succeeding decades to those considered in "Chemistry in Old Philadelphia."

G. M. B.

MANUAL OF LABORATORY PRACTICE FOR STUDENTS OF PHARMACY.

By George B. Kaffman, BSc., Ph.D., James H. Beal, D.Sc., Phr.D., and Julius A. Koch, Ph.D., Phr.D. Third edition, 92 pages, interleaved. Published by The Midland Publishing Company, Columbus, Ohio. \$1.50 plus postage.

A new edition of this laboratory guide for pharmacy students has just been published. The table of contents indicates its scope: "Physical operation," embracing weights and measures, specific gravity, the use of heat, melting and boiling points, and distillation. Then about 35 illustrations of "galenical preparations," followed by manufacturing processes for a number of simpler "chemicals."

Part 4 offers about 35 "prescriptions" for compounding, which have evidently been selected to give the student experience in the filling of a variety of types. Parts 5 and 6 take up "chemical laboratory methods," first those related to volumetric analysis, then gravimetric. In the last chapter "pharmaceutical assaying" is considered, including alkaloidal preparations, formaldehyde, spirit of nitrous ether, pepsin and pancreatin.

A guide of this character is doubtless a time saver for the instructor of a laboratory, and makes it easy for the student to carry out the work assigned, but it is doubtful if any two group of men would select the same types for galenicals or prescriptions, to illustrate pharmaceutical practice, and, with the exception of the outlines for some of the physical operations, the prescriptions selected

for practice, and a number of the manufacturing chemical processes, the operations are identical with those in the U. S. P. or N. F.

By many it is believed best for a student to work directly from the official guides as in that way much greater familiarity is obtained with other parts of the text as the "rubrics," tests, doses, etc., and also with other preparations of the same class, and when the student himself is required to reduce the formulas to a workable laboratory quantity, he secures valuable practice, confidence in his ability to use the Pharmacopœia, and an emphasis upon the formula.

The directions given in the manual are usually verbatim with, or at least follow the style of the U. S. P. or N. F. One feels that an excellent opportunity to introduce explanations, reactions and more detailed instructions or desirable cautions, has been missed. It is a surprise to find no less than four fluid extracts among the few galenicals given, while such desirable and important preparations as solution of magnesium nitrate, ointment of rose water, hydriodic acid and its syrup, etc., are not included.

On the whole, no doubt, a manual of this character serves a useful purpose for the school where it is developed and may be suggestive elsewhere, but its limited scope, lack of flexibility and failure to provide for that element of personal selection, expansion and initiative, which is an important quality of every efficient teacher, will probably restrict its use mainly to its authors own field of activity.

E. F. C.

A CRITICAL REVISION OF THE GENUS EUCALYPTUS. By J. H. Maiden, I.O.S., F.R.S., F.L.S., Government Botanist of New South Wales and Director of the Botanic Gardens, Sydney. Vol. IV, Part 6. Published by the Government of the State of New South Wales.

From time to time, the parts of this classic monograph have been reviewed in the pages of the AMERICAN JOURNAL OF PHARMACY as they have been received. The part now at hand continues in the same excellent and scientific style as in the preceding parts to present with fine illustrations seven distinct species of Eucalypti along with such varieties as are recognized.

The species considered are *Eucalyptus occidentalis* Endlicher and variations from the normal description worthy of considera-

tion as of varietal rank; *E. macrandra* F. v. M.; *E. salubris* F. v. M.; *E. cladocalyx* F. v. M.; *E. Cooperiana* F. v. M.; *E. intertexta* R. T. Baker; *E. confluens* W. V. Fitzgerald.

G. M. B.

## ✓NEWS ITEMS AND PERSONAL NOTES.

✓✓AMENDMENT TO THE NEW JERSEY PHARMACY LAW.—At the recent session of the New Jersey legislature section 6 of the Pharmacy Practice Act, which is the section of the law relating to the disposition of poisons, was amended. The amendment adopted in reality rewrites the entire section and handles this subject in an up to date manner. The revised law provides that it shall be unlawful to sell or deliver to a minor under twelve years of age or to any person of unsound mind or under the influence of liquor any poison. The poisons are classified under schedules A and B. The former including substances commonly recognized as "deadly poisons" and which according to standard works are liable to be destructive of adult human life in doses of five grains or less. The seller is compelled to learn that the person to whom delivery is made is aware of the poisonous character of the substance and is a proper person to purchase such a poison and that the intended use is legitimate and to keep a record of such sale setting forth the date and hour, the article and quantity delivered, the use stated, and the name and address of the purchaser.

Schedule B enumerates the less toxic substances, many of which are commonly employed in domestic practice, agriculture, and the industries and any other substances which according to standard works, while not considered as toxic in doses of five grains or less is, nevertheless, liable to be destructive of adult human life in doses of sixty grains or less.

Other new provisions of the act are, making as duties of the Board of Pharmacy the printing and distribution of schedules of poisons and the antidotes approved as the most suitable for the various poisons. The board is to have power to revise and amend such schedules from time to time.

✓✓AMERICAN DRUG MANUFACTURERS' ASSOCIATION.—The eighth annual meeting of this association was held in New York City, the



following officers were elected for the coming year: *President*, R. C. Stoffer; *Vice-Presidents*, F. B. Kilmer, Willard Ohliger, Burton T. Bush; *Treasurer*, Franklin Black; *Secretary*, W. J. Woodruff. Mr. W. A. Sailer and Mr. J. E. Bartlett were elected as members of the Executive Committee and Mr. Chas. M. Woodruff was appointed chairman of the Legislative Committee.

The action taken at this meeting relating to the proposed "Federation of Pharmacy" was incorporated in preambles and resolutions, setting forth the reasons which in the opinion of the members of the association made it impractical for its membership to approve of the federation as proposed. The following paragraph from the resolutions sums up their main objection to what is termed the "inherent incompatibility of such a Federation."

"*Resolved*, That with the best of feeling and friendliest sentiment toward all other independent pharmaceutical associations, as well as with the utmost respect for the sources of the federation idea, the American Drug Manufacturers' Association hereby declares that it cannot shift the responsibility of conserving the lawful interests of the men and women who are the stockholders of its constituent members to the shoulders of a Federation; nevertheless the Association will hold itself receptive of any plan of useful and lawful coöperation that will not involve the surrender of its independence or interfere with its freedom of action."

One of the important questions discussed at this meeting was that of "Trade Acceptance." This proposed innovation in American business methods, which is being advocated by many commercial organizations, was presented both pro and con. Mr. Howard Marshall, of Joseph Wild & Co. of New York, presenting arguments in favor of the proposition and Mr. Webster King Wetherill, of the Aldine Trust Company of Philadelphia, some in opposition.

Dr. J. M. Francis, of Detroit, argued in favor of the retention of the product patent on medicinal discoveries. This question is another problem that has been debated for several decades in medical and pharmaceutical circles and on which self interest seems to be a dominating factor for the opinion held.

✓  
THE MANUFACTURING PERFUMERS' ASSOCIATION.—This progressive organization of manufacturing perfumers held its twenty-fifth annual convention at Biltmore Hotel, New York, on April

22 and 23. The able address of the president, Mr. G. A. Pfeiffer, reviewed the important problems affecting their industry and the difficulties that have been so greatly increased by reason of the war and the taxes resulting therefrom.

A number of interesting papers were presented, that by Mr. Christian Beilstein of the firm of Dodge & Olcott on "Raw Materials" being among the notable topics discussed.

Mr. G. A. Pfeiffer was reëlected as president; Mr. Francis W. Jones was elected as vice-president.

MESSRS. ✓FRITZSCHE BROTHERS INCORPORATED.—Fritzsche Brothers of New York who have long been established as among the leading manufacturers and importers of essential oils, aromatic chemicals, drugs, and perfumers materials, have been incorporated under the laws of the State of New York with a capital of \$1,000,000.00.

The officers elected are: *President*, F. E. Watermayer; *Vice-President*, F. H. Leonhardt; *Secretary*, Julius Koehler; *Treasurer*, Wm. A. R. Welcke. The main reasons for incorporating assigned are the desire to perpetuate their long established good will and business and to afford an opportunity for some of their old employees to become interested. Mr. Leonhart has been with this firm for twenty-five years and Mr. Koehler's connection dates back thirty-two years and that of Mr. Welcke thirty-four years.

FURTHER CHANGES IN THE MANAGEMENT OF THE H. K. ✓MULFORD Co.—Mr. A. Homer Smith, who served as assistant to the chief of the medical sector of the Council of National Defense during a considerable portion of the war, has been made secretary of this company and also the general sales manager. Mr. Smith is a native of Smyrna, Del., and is a graduate of the Philadelphia College of Pharmacy. In 1905 he engaged as a salesman with the H. K. Mulford Co. His energy and ability, coupled with good nature, tact and diplomacy, has brought to him continuous advancement and success.

Mr. A. E. Wills, formerly in charge of the London office of the firm and later the district manager in Boston, has been made assistant sales manager and transferred to the Philadelphia office.

✓DR. FISCHELIS IN THE ADVERTISING FIELD.—Dr. R. P. Fischelis, the genial secretary of the Pennsylvania Pharmaceutical Associa-

tion, has severed his connection with the H. K. Mulford Co. and has associated himself with the Matos Advertising Agency of Philadelphia. He expects to give his personal attention very largely to the placing of advertisements of the drug and chemical interests.

THE GOLDEN ANNIVERSARY OF THE CLASS OF 1869.—Mr. James S. Robinson, Ph.G., still engaged in business as "apothecary," 22 N. Second Street, Memphis, Tenn., recently addressed a letter to Mr. Adam Pfromm, of Philadelphia, a fellow classmate of the class who were graduated from the Philadelphia College of Pharmacy on Tuesday morning, March 23, 1869, the first class graduated from the college after the opening of the new building, in which he writes:

"The enclosed speaks for itself—fifty years since this class went out of the new college. I thought it might be put in the JOURNAL to see how many are still in the business."

The "enclosed" is the following list of names of the graduates.

GRADUATING CLASS OF THE 48TH SESSION, PHILADELPHIA COLLEGE  
 OF PHARMACY.

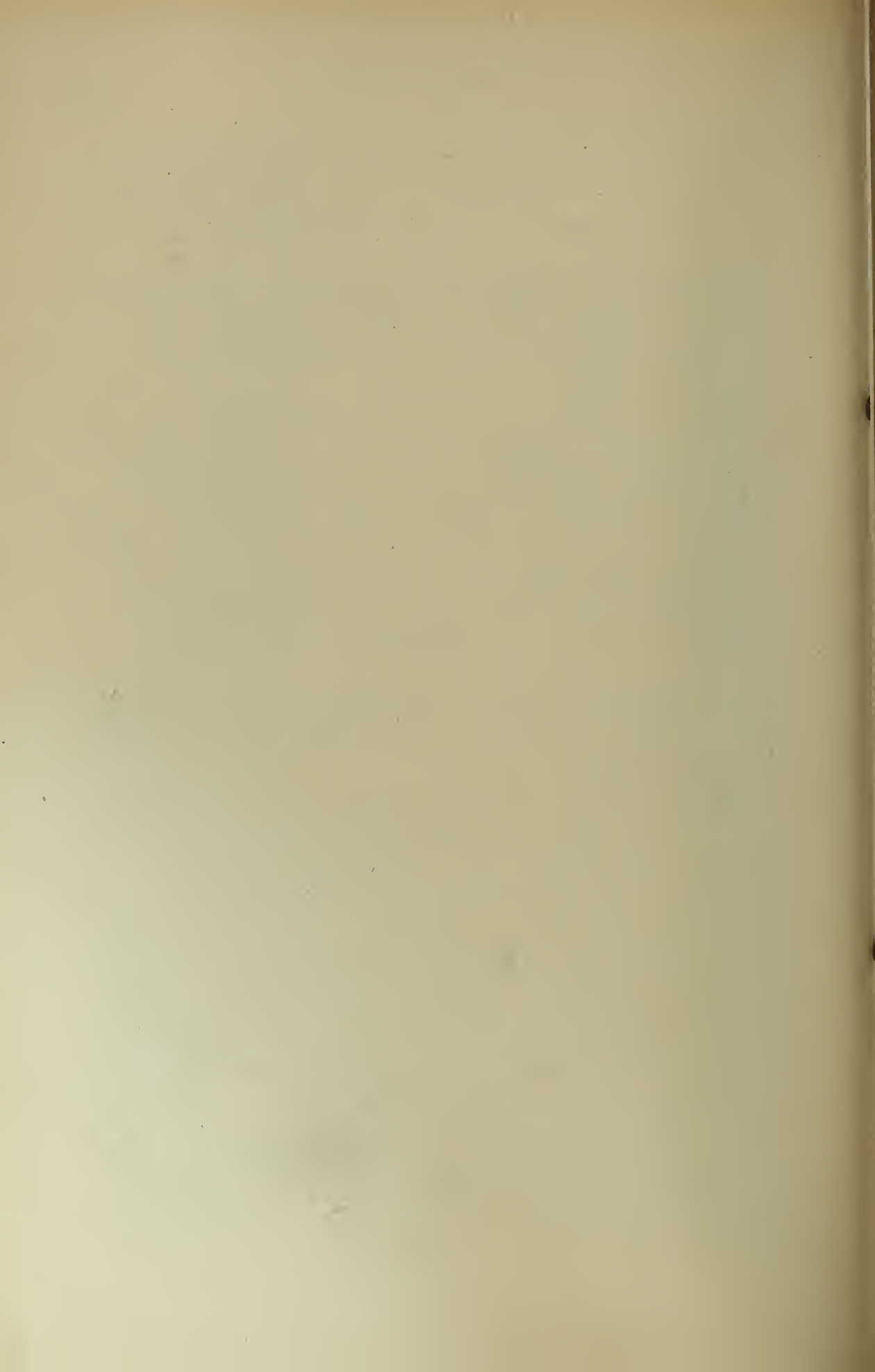
LOUIS A. BATES .....	Montgomery, Ala.
JAMES S. BELL .....	Albion, Canada.
HENRY K. BOWMAN .....	Philadelphia, Pa.
JOSEPH J. CUMMINGS .....	Philadelphia, Pa.
JAMES CRAVEN .....	Philadelphia, Pa.
AARON R. DAVIS .....	Allentown, Pa.
HENRY H. DAVIS .....	Crosswicks, N. J.
JOHN H. DeHUFF .....	Lebanon, Pa.
CHRIST. ED. EYSTER .....	Chambersburg, Pa.
JAMES G. FRITCHEY .....	Lancaster, Pa.
CARL FRÜH .....	Philadelphia, Pa.
CHARLES HAND .....	Burlington, N. J.
CHARLES E. HOLSTEIN .....	Norristown, Pa.
THOMAS J. HUSBAND, JR. ....	Philadelphia, Pa.
HAMILTON HUTCHISON .....	Philadelphia, Pa.
G. W. ISARD .....	Philadelphia, Pa.
D. AUGUSTUS JONES .....	Mount Holly, N. J.
CLEMENT KELTY .....	Salem, N. J.
GEORGE W. KENNEDY .....	Pennsylvania.
C. H. KOLP .....	Pennsylvania.
WM. E. KREWSON .....	Abington, Pa.
EUGENE LAMPARTER .....	Germany.
CHARLES H. MERKLEIN .....	Chambersburg, Pa.
WM. W. MOORHEAD .....	Germantown, Pa.
AULAY W. PECK .....	Philadelphia, Pa.



STEPHEN F. PENROSE .....	Quakertown, Pa.
ADAM PFROMM .....	Philadelphia, Pa.
FREDERICK H. PHELPS .....	Jackson, California.
FERRIS PRICE .....	Philadelphia, Pa.
MILTON RAMBO .....	Chester, Pa.
CHARLES B. READ .....	New Jersey.
JOHN J. REYNOLDS .....	Chambersburg, Pa.
WILLIAM T. RIDGWAY .....	Mount Holly, N. J.
HENRY E. ROBERTSON .....	Philadelphia, Pa.
JAMES S. ROBINSON .....	Philadelphia, Pa.
ROBERT C. SHARP .....	Pennington, Pa.
JACOB H. STEIN .....	Annville, Pa.
J. SCOTT STORKS .....	Philadelphia, Pa.
HARRY B. TAYLOR .....	Philadelphia, Pa.
L. ALPINUS TREICHLER .....	McKeansburg, Pa.
CHARLES B. UNSICKER .....	Cincinnati, Ohio.
JARVIS R. WALLEN .....	Bridgeton, Pa.
FRANK WARE .....	Bridgeton, Pa.
SAMUEL F. WARE .....	Bridgeton, Pa.
HARRY B. WEYMER .....	Philadelphia, Pa.
EDWIN K. WILSON .....	Haddonfield, N. J.
CHARLES WIRGMAN .....	Philadelphia, Pa.
ISAAC G. WOLFE .....	Philadelphia, Pa.

The editor hopes to have a few lines from each surviving member for publication as well as to warm each others' hearts "with the joys of the days gone by."

✓  
 LEHN & FINK, INC., OWNERS OF THE TRADE MARK "PEBECO TOOTH PASTE."—Since 1903, Messrs. Lehn & Fink, of New York, have been manufacturing Pebeco Tooth Paste at their laboratory in Brooklyn under an agreement for the payment of a royalty to the German firm originating the preparation and trade mark. When the United States entered the war against Germany, the Federal Trade Commission granted to Lehn & Fink the sole right of manufacturing and marketing this preparation in the United States. The records as published show that for several years prior to the war the royalty paid to the German firm amounted annually to more than \$100,000. The Alien Property Custodian having seized as enemy property the trade mark and trade rights, these were sold at public auction on April 26, to Messrs. Lehn & Fink, the only bidders, their priority rights and trade interest being respected by the other manufacturers of pharmaceutical and toilet articles. The price bid was \$1,000,000.



# THE AMERICAN JOURNAL OF PHARMACY

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JUNE, 1919

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## EDITORIAL.

### WHO WILL BE THE LEADER?

In connection with our editorial suggestion for the organization of a commission, to be composed of representative "Committees on Fraternal Relations" appointed by the national organizations of the several branches of the medical practice, whose special duty was to be the "regeneration of the medical practices" a reformation that would bring about a closer relation among them and a correlation of their services and the elimination of unethical practices and encroachments, the question has been propounded; Which of these national associations should take the lead in such a movement?

That the time is opportune is apparent. The need for the reform is conceded. The benefits accruing to the medical practices and the improvement in their services rendered to humanity thereby, cannot be gainsaid. The progress assured and the improved standing of the medical professions justifies immediate action.

If the suggestion be approved, if the inherent value of such a procedure be fully appreciated and the desire to test the feasibility of the plan be sincere, the mere question of who shall take the initiative becomes of secondary importance. Coöperation is the essential key note to the successful development of this ideal and coöperation must mean equal interest, equal support, equal sincerity, equal earnestness and enthusiasm of all of the branches of medical practice.

Medicine as the oldest of these established branches could with merited honor, take the lead through its powerful organization the American Medical Association. On the other hand the American Pharmaceutical Association, as the representative organization of



ethical pharmacy, could with no impropriety assume the responsibility of proposing such a reorganization of medical practices. The opportunity for the rendering of a truly altruistic service that will redound to the benefit of society and also to the advancement of the professions concerned, is presented and there should be no hesitancy on the part of the professions and the organizations representing them in organizing and promulgating such a movement.

G. M. B.

### THE REPEAL OF THE LUXURY TAXES.

When Congress entered upon the preparation of the Revenue Law of 1918, the members were confronted by the necessity of raising enormous sums to carry on the war for a period variously estimated as from a few months to several years. Consequently, their attention was directed to the imposing of excise and luxury taxes upon all sorts of articles, some of which had never before been considered by Congress as worthy of consideration for taxation. Although the armistice was signed at a date much earlier than was generally anticipated, the discussions in Congress and the various contentions and problems entering into consideration in the framing of a revenue law, had progressed to a point where entire reconsideration, in the uncertainty existing, was impractical and so in the Act, as passed finally in February, 1919, we find many inconsistencies and much that is to be criticised and some sections that will require amendment or repeal.

In the supposed exigency, the loyal people of the United States accepted the decisions of Congress and as a body have very generally met all demands and borne the burden of very unusual and heavy taxation. Now that the clouds of war are rolling by and peaceful skies spreading overhead and the trade winds of industrial and commercial activity and national progress blowing our way, conditions have undergone a radical change.

The time has come to take more sober thought, to pass more deliberate judgment upon what are proper articles to be selected for taxation. The evident intent was to select for special taxation articles which were considered as unnecessary, simply for adornment or self-indulgence, the consumption of which could be curtailed or a special tax paid by those who persisted in purchasing such finery and luxuries.

With this theory and purpose of the enactment we are finding no fault, but with the practical application and the selection of articles on which special taxes are levied, we are of the opinion that Congress committed many errors calling for criticism and the demand for prompt correction. We cannot believe that the exigency confronting Congress justified the placing of special taxes upon such articles as unfermented grape juice, carbonated waters, ice cream and soda-water, or upon medicines because held out by the manufacturers as remedies for any disease "affecting the human or animal body," or upon "toilet soaps" for maintaining a healthy bodily aspect, or upon petroleum jelly, hair restoratives, mouth washes and dentifrices, all of which play an important part in modern hygiene. Scientific sanitation considers many of these as necessary agents and their daily use as essential to the preservation of health.

The action of Congress in making such articles special objects for taxation places before contemporary nations, our friends and allies as well as our enemies, a condition of exigency and necessity that never existed in the United States and this false impression cannot be eradicated too soon. The sentiment is very pronounced that Congress erred in the placing of these so-called luxury and special excise taxes and the demand for their repeal is unmistakable and must receive the early consideration of that body.

In our opinion the excise taxes covered by Title IX with its various sections covering such a variety of articles as automobiles and accessories so essential to business, musical instruments, sporting materials, portable fans, thermos bottles, furs, boats, toilet soaps, carpets, trunks, wearing apparel, jewelry, etc., should be carefully revised to discriminate between such necessities as toilet soaps, to encourage the use of which no tax should be levied, and jewelry for adornment only. Moreover that section 628 taxes on carbonated waters and soft drinks; 630, that on ice-cream, sodas, sundaes, etc.; and 907, perfumes, toilet articles, petroleum jellies, hair preparations, mouth washes, dentifrices, proprietary medicines, etc., should be repealed in their entirety, and the sooner the better.

G. M. B.

## THE COLLEGE COMMENCEMENTS AND THE PHARMACEUTICAL ASSOCIATIONS.

The passing of time has brought us once more to that period of the annual calendar that marks many events of pharmaceutical interest. In the early summer months the principal schools of pharmacy have their graduation exercises and these commencements note the entrance of new units into the service of pharmacy. About this season of the year, many of the state pharmaceutical associations, likewise, meet in annual convention, and the various sections and committees of the American Pharmaceutical Association are rejuvenated in anticipation of its sessions.

Someone inquires wherein is the relation of these events and the connection between these two subjects? There is a distinct link between these two different occasions and events pharmaceutical that should be so welded together as to form an inseparable interlocking.

The members of each graduating unit should be thoroughly imbued with the sense of the responsibility of the vocation in which they are about to enter and with loyalty to the traditions and precepts of the profession. The very first lesson that should be instilled into the mind of the young pharmacist is that he is engaging in a vocation of professional service to mankind. That the faithful discharge of this service will require continual study and acquaintance with the highest ideals which he will find only in associating himself with the leaders of his profession. Only by becoming a member of the pharmaceutical organizations will he keep in touch with these and learn that only by coöperative professional work is the best possible service achieved and also the greatest benefit accrued to the individual contributors.

The value of the associations, local, state and national, in the development of the individual pharmacist and the share of responsibility falling to each member of the calling should be impressed on the new graduate and at the very first meeting after graduation he should be initiated into membership and assume a part in such association work.

G. M. B.



## SOME OF THE DEFECTS IN THE MANAGEMENT OF THE AMERICAN PHARMACEUTICAL ASSOCIATION.

"Whatever thou hast to take, that take thou quickly;  
Give quickly what thou hast to give; do quickly  
The work thou hast to do; if thou delay  
Time will drink up the spirit of thy act."

There is probably no desire so universally held by the pharmacists of America as that earnest wish to advance the welfare and progress of the American Pharmaceutical Association. The earnestness of our desire, the enthusiasm of our efforts, however, should not blind us to the errors that have become engrafted upon its methods. On the contrary, our concern for its interests and advancement fully justifies the calling of attention to defects the correction of which becomes necessary if our association is to fulfill its aims and objects. Love for an association that has bestowed upon the writer its highest honors and office has deterred and delayed public criticism for a long time, and coupled with this has been the fear that such criticism would be misunderstood or the motives actuating this be misconstrued. The world never has and never will love cowardice, either physical or moral, and the conviction has grown that duty demands that attention be directed to certain well-developed evils in order that reform may be accomplished.

The American Pharmaceutical Association, by reason of its composite membership, is in a position to combine and coördinate the best efforts of pharmacy in the attainment of any desired object and therein is the great opportunity of this organization to serve both the professional and commercial advancement of pharmacy.

If one read over the addresses of its presidents for only a limited period,—we will say of the last ten years,—he becomes cognizant of the many topics of vital importance to pharmacy that have been thus brought to the attention of the association. If he further follows up the consideration received and the action taken as set forth in the published proceedings of the meetings he will learn that in most of these matters the association has by *resolution* taken appropriate action or directed that certain duties and services to pharmacy should be performed by some one or by some committee. Then WHAT? Frequently *that is the end*.

A single example is cited, and this can be multiplied very many times in matters of material importance. Five years ago, the presidential address set forth that "The nation-wide adoption of a legal requirement that every pharmacist must be a graduate of a school of pharmacy before being licensed to practice, is the very first step essential for the professional elevation of pharmacy." "It remains as an initial duty of this association to see that this condition is changed and changed promptly." His recommendation that a committee be appointed to agitate this question and to procure in each state the enactment of a pre-requisite law, was endorsed by the Committee on President's Address and later approved by the association. It is not known that any further action has been taken and this important subject has lain dormant, buried in the graveyard of resolutions, while prominent members of the association have been writing lengthy epistles upon the lack of professional standing of pharmacy. One year of real, live, activity will out-balance a century of resolutions.

"To carry out an enterprise in words  
Is easy, to accomplish it by acts  
Is the sole test of man's capacity."

The causes of this lack of action and the consequent loss of opportunity and prestige are not hard to find, nor should they be difficult of correction. Delay, procrastination, are evident factors and the advice from the Code of Manu, quoted in the introductory paragraph is quite appropriate.

A structural weakness in the methods of the American Pharmaceutical Association is the absence of a plan that will provide for the continuity of its efforts. After a member has been elevated to the high office of president, he takes very much to heart the welfare of the association and makes a careful study of its plan and possibilities of service to the vocation of pharmacy and to the public. He prepares a well thought out address embodying his suggestions for improvements and changes, presides at a few meetings of the annual session and then passes the gavel of authority to his successor. His recommendations may have been favorably considered and approved by the few members present at the final session, there has not been provided, however, the adequate means for enforcing or putting these into accomplishments. His successor is likely to repeat the same course of procedure.

The machinery is rattling somewhere. It needs tightening up and adjustment and at least one new part. It should be made as a stated duty for the new president or else for the chairman of the council to see that there be established the lacking coördination and continuity of service that is essential to the success of its undertakings. With a multitude of committees and its numerous activities a strong guiding hand is needed that will insure continuous action and stop the delay and misspent energy. Either the power of the executive officer, the president, must be extended by the by-laws or an executive committee created with the necessary power.

G. M. B.

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SECRET—PRIVATE—PERSONAL.

(No. II—PRIVATE.)

BY JOHN URI LLOYD, PHARM.,

CINCINNATI, O.

*Private.*—Come, with this word, phases of definition in both pharmacy and medicine, apart from those recorded by almost any recognized authority. In this writer's opinion, the artificial construction localized in both the medical profession's code and the by-laws of the art of pharmacy needs be relieved from any touch of opprobrium when the word "private" is properly employed. Its use, as given by nearly every recognized authority, shatters no professional or commercial ideal that recognizes the right of anyone to a privilege in ambition's advancement of both self and others, in science, profession or art.

The "odium" attached to the word *private* in both medicine and pharmacy is well deserved from one view, *i. e.*, when it concerns the impostor, and in this direction should not be abandoned. But no authority, whether independently legal, ethical or lexicographical, attaches to the word a blanket stigma.

Note a few definitions of the word, as recorded by Webster :

*Private a.*—Belonging to, or concerning, an individual person, company, or interest; peculiar to one's self; unconnected with others. *personal*; one's



own; not public; not general; separate; as, a man's private opinion; private property; a private purse; private expenses or interests; a private secretary.

Not publicly known; secret; as, a private negotiation; a private understanding.

*Private, n.*—A secret message; a personal unofficial communication.

*In private*, secretly; not openly or publicly.

To apply these, fairly, to pharmacy or to medicine shocks no ethical sensibility, if claims for "occult" superiority or unwarrantable pretensions be avoided. A physician is warranted in having *private* opinions concerning therapeutic problems, and, so far as this writer can perceive, he has a right either to maintain them in his own practice or announce them by open discussion, as he personally elects. But to herald to the world unwarranted claims for possession of exceptional qualifications is as improper as for a bank to announce the possession of capital that does not exist. To each the common law of ethics alike applies—the word private is debased if complicated with falsehood.

It may be forcibly argued that the profession of medicine is a humanitarian cult, that of the banker, materialistic; that the physician is not in general business and has no right to anything private, regardless of personal needs or professional opportunities. To this some might answer, the establishing of a personal conspicuity that makes self-deputation, is in itself a personal *business* service; that the physician who makes a superior reputation either in diagnosing a class of ailments, or in the treatment thereof and announces the fact, brings to himself the return of merit from other afflicted persons, who prefer to trust the successful *originator*, even though the process of treatment and the agents employed are by him broadly published. It might be argued that the more widely a surgeon publishes his processes and reports successes, disclaiming anything private, the more cosmopolitan becomes his personal opportunity.

*Publicity* means *business*. Again, one might argue, as concerns the public's responsibilities to a benefactor, that it is sophistry to attempt to draw a distinction between the iron-monger who serves the people and profits thereby, and the physician who likewise devotes to them his care and thought, taking a fee therefor. If the iron-monger succeeds in accomplishing something of general value, through private or patented processes, the people, including physicians and surgeons, pay the bill. In like manner, if the physician or surgeon makes discoveries that are valuable, he should be financially

recompensed, if publicity for the general good is accorded. In such views as these, each party to the discussion may in all fairness take a part.

However, most insidious, often approaching sophistry, are such arguments, carried to the extreme, in some of their ethical, as well as material outreaches. That physicians or surgeons should be required to publish the details and results of every operation or diagnosis, is not acceptable to some persons. That *privacy* is occasionally a right of everyone, and especially in such as this, is a self-evident, ethical axiom. To announce openly, much less publish, the closet discussions of a called consultation of physicians, or surgeons, might do much harm. *Privacy* such as this seems to be a sacred trust; likewise, privacy concerning the diseases from which some persons suffer.

Turn now to the pharmacist who in *business* has no professional fee, but who joins hand with the physician in his contribution to humanity's welfare. Might one not argue that, on ethical grounds, no one should deprive him of rights accorded in common law to other business men, or expect from him greater contributions to humanity than come from others dependent on scientific art for a livelihood? Might one not ask, should he not have the fullest self-privilege and protection, by reason of his personal (*private*) efforts to excel? Might it not be asked, is not the accomplished pharmacist entitled to even greater *personal* privileges than others? Is he not an educated man and yet dependent wholly on the materialistic side of his profession or art for his opportunity to serve the people? Is not the pharmacist who devotes his early youth to pharmaceutical *education*, who in later years spends his money, often the savings of a lifetime, to the limit in acquiring knowledge, confronted with competitors no less unworthy than the charlatan who discredits the term physician? Why should anyone deny him the returns that he has earned, and that cannot in some instances come unless he keeps *in private*, details that the charlatan neighbor has not acquired? In this line, *is not knowledge property*? Might it not be argued that one of the reasons why young people take a pharmaceutical education or spend time and money in research, is to enable them to become superior in their art? Is not every qualified pharmacist, be he young or old, who has by sacrifice earned his privilege to the position, surrounded by competitors with larger signboards over

their doors, whose advertisements to the public are such as he is, as a rule, ethically denied.

Summing it up from this angle it might be argued that *private* processes earned by educational accomplishments by a legitimate pharmacist (even the method of compounding a "face lotion" or an elastic pill) take nothing from others, and that neither law nor justice would demand that a pharmacist deny himself the privilege of fair business returns through such *privacy*. Does not this view prevail throughout the length and breadth of the land, in the judgment of the public generally, and is it not also most generously accepted by the practicing members of the profession of medicine? The physician naturally, as he should, recognizes the fairly-earned *art* of the qualified apothecary, that gives him an individuality. He comprehends that this man of many sacrifices has earned the right to the moderate materialistic return that comes from a superiority bred by self-effort. He gladly gives to him his professional confidence, and considers it his privilege to recognize merit earned by educational sacrifice. He comprehends that the operating pharmacist is not a recompensed teacher of others; that no professional fees, paid for professional services, are his part; that his duty to the world is best accomplished in continued private efforts, the material results of which he can apply to self-service or freely give to the world, as he so desires.

And—this writer also believes that the aim of the faculty of every college of pharmacy is so to instruct the students that they may have this superior advantage and that their after-lives may thus be made less irksome. They comprehend that the pharmacist is of all others a laborer of great responsibility, and that to him who thus serves others, with little recompense at the best, applies the Scriptural injunction, "The laborer is worthy of his hire."

But—and this writer uses now the first person, so his own position be not misunderstood—no pharmacist, if he so desires, should be denied the privilege of *instructing* others, even to the wrecking of his *private* interests. In this I go even further; the *art* of pharmacy, the prosperity of the pharmacists of America, both dispensing and manufacturing, rest largely upon sacrifices made of *private* opportunities, by teaching pharmacists of the olden time; self-sacrificing pharmacists, who, in the privacy of their shops and homes, toiled, accomplished, gave and taught. The names of a great number come



now to memory. The faces of these exemplary men rise successively before my eyes, as I pen these lines. And also come, unbidden, the faces of not less sacrificing, not less modest pharmacists, who today are worthily utilizing, for the benefit of others, the wealth handed down to them as a sacred trust. And yet, I believe that such processes are *privileges*. That if an apothecary makes a discovery that benefits humanity it is often a *duty* to utilize it to the financial advantage of his family and himself, and that no law of just ethics can demand that he give such property, without recompense, either to his competitors or to the world at large.

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## THE COLLECTION AND SOME USES OF THE OLEORESIN OF DOUGLAS FIR (OREGON FIR BALSAM, DOUGLAS FIR TURPENTINE).

BY S. A. MAHOOD,

*Chemist in Forest Products, Forest Products Laboratory, U. S. Forest Service, Madison, Wisconsin.*

While the oleoresin of Douglas fir (*Pseudotsuga taxifolia*) is the chief, if not the only, constituent of an article of commerce regularly listed under the name of Oregon fir balsam, there is but little information available on the methods employed in collecting this material. The facts at hand or obtained from those familiar with the gathering of this product indicate that the oleoresin is obtained in one of two ways.

### DRAINING METHOD IN LUMBERING OPERATIONS.

One of these methods consists in having buckets or other suitable receptacles where logging operations are being carried on and in allowing the oleoresin which exudes from some trees when they are felled to drain into one of these vessels.

### CRUISER METHOD BASED ON SPOTTING TREES.

The other method is used by those who make a business of collecting this material. A wind shake in a standing tree produces a pocket which in time fills with oleoresin, and, if an aperture is made in the pocket, the oleoresin readily flows out. These professional

collectors travel through the woods until they "spot" a tree having a cavity containing oleoresin. A hole is bored into it and the pocket drained, the oleoresin being conveyed by means of a tube into suitable containers. From one to three gallons are frequently obtained from a single boring. There is very little, if any, evidence that a given tree contains such a pocket, but those who make a livelihood as collectors claim to be able to "spot" such trees and they meet with a fair degree of success. It is apparent, however, that there is the element of chance in such a method and the collectors often go a whole day without making a single productive tap.

It is evident from the foregoing that the methods of collecting this material might possibly be improved. It might be supposed that the oleoresin could be obtained by chipping the tree according to the method employed in the South for obtaining ordinary crude turpentine. This method, however, when applied to Douglas fir, gives very little resinous material.

Since the oleoresin tends to collect in pockets formed by accident inside the tree, it seems reasonable to suppose it would also tend to collect in pockets formed by design. In other words, the method employed on the slopes of the Alps for obtaining Venice or Larch turpentine might presumably be applied to advantage in securing Douglas fir turpentine.

#### EUROPEAN METHOD A SYSTEM OF TAPPING.

This method<sup>2</sup> is based on the fact that in the European larch the oleoresin tends to collect in the heart of the tree<sup>3</sup> and that it often fills the cavities made in the trunk by frost or other causes. One or two holes, 1 to 1½ inches in diameter and horizontal or nearly so, are bored by means of an auger early in the spring in mature trees about forty inches in girth. They extend to the center of the tree and are about a foot from the ground. The holes are carefully cleaned and then closed with a dry larch plug to prevent loss by evaporation. In the autumn the cavities are emptied by means of an auger. After the second or third collection, the holes are widened to 1.6 inches. In some sections the holes are not plugged, but wooden tubes are inserted in the openings and the oleoresin allowed

<sup>2</sup> "Die Oesterreichischen Alpenlander und ihre Foreste," page 369; *Archiv. der Pharmacie* (1900), page 389.

<sup>3</sup> *Botanische Zeitung*, 17, pages 329 and 377.

to flow through them into suitable receptacles.<sup>4</sup> The production once begun entails little labor and the product obtained is quite pure. The trunk of the tree is injured but little and the same cavities are said to yield oleoresin for twenty<sup>5</sup> to fifty<sup>6</sup> years.

#### COMBINED CRUISER AND TAPPING SYSTEM.

The European method might be used to advantage in combination with the "cruiser method" mentioned above by plugging the tap from which no oleoresin flows immediately and draining the tap the following season or sooner if the accumulation of oleoresin takes place rapidly enough. The labor involved in making the tap would not then be entirely lost. Instead of being plugged, the tap might be connected to some suitable container and allowed to drain for a given period. In that case care should be taken through the use of a closed vessel to prevent loss from evaporation. In addition to living trees, the stumps of recently felled trees may often be tapped to advantage.

#### COMMERCIAL USES OF OLEORESINS.

The demand for Oregon fir balsam seems to be on the increase, as indicated by the present (February 1, 1919) market price of \$1.75 to \$1.80 per gallon, as compared with \$1.15 to \$1.25 some time ago. This increase in price has been the result of increased domestic demands, as there has been little, if any, export trade in this article since the beginning of the war. The domestic consumption is on the increase and this is due apparently to a greater use of this material, particularly by the varnish trade. Oregon fir balsam is also being used to some extent as a substitute for Venice turpentine, a purpose for which, under the name of Douglas fir turpentine, it was suggested by the Forest Products Laboratory about two years ago. As such it is employed particularly in the ceramics industry and in the manufacture of porous plasters.

In addition to these uses, it is probably employed to some extent also in the place of Canada balsam. The term "balsam," however, as applied to both of these articles, is a misnomer, since they are not balsams but turpentine. Oregon fir balsam has been regarded

<sup>4</sup> Duhamel, "Traite des Arbres," II, page 355.

<sup>5</sup> Tschirch, "Die Harze und die Harzbehalter" (1906), page 614.

<sup>6</sup> G. Planchon et E. Collin, "Les Drogues simples d'origine Vegetable," I, page 70.





View of larch tree tapped for Oleoresin according to the European method.

with suspicion as a substitute for Canada balsam, especially since the publication of an article by Dowzard<sup>7</sup> purporting to show that Oregon balsam is a fictitious article "made by dissolving colophony in turpentine." He regards the acid number of the resin (non-volatile residue) as indicating that Oregon balsam contains colophony, since the two values are:

Oregon fir balsam resin .....	153
Colophony .....	155

More recent work by Rabak<sup>8</sup> on commercial samples and of Schorger<sup>9</sup> on authentic samples of Oregon fir balsam show the acid values of the resins (non-volatile residues) to be practically the same. The former obtained an average value of 153 (calculated basis of 70 per cent. resin) and the latter of 166 (calculated). It follows, therefore, that a high acid value for the resin does not show Oregon fir balsam to be a spurious product as assumed by Dowzard. On the other hand, it apparently does differentiate Oregon fir balsam from Canada balsam. The constituents of these two products, so far as they have been determined are, however, quite similar, and it is probable that in practice Oregon fir balsam will, in many cases, serve the purpose quite as well as Canada balsam and at about one sixth the cost.

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## THE PHARMACY AND MANNER OF USE OF TETHELIN.

BY GEORGE E. EWE.

Tethelin is a substance partaking of the nature of a lipid, derived from the anterior lobe of the pituitary body, and was first isolated by T. Brailsford Robertson, Ph.D., D.Sc., in 1916. It has been suggested by Robertson<sup>1</sup> as being the growth-controlling principle of the anterior lobe of the pituitary body.

<sup>7</sup> *Chemist and Druggist* (1904), page 64; Allen, "Commercial Organic Analysis," IV, 79 (note).

<sup>8</sup> *Pharmaceutical Review* (1904), 22, 293.

<sup>9</sup> *Journal American Chemical Society* (1917), 39, 1040.

<sup>1</sup> Robertson, T. B., *Jour. Biolog. Chem.*, 1916, XXIV, 397, 421.



## OBJECT OF THIS PAPER.

Tethelin is an extremely sensitive substance; even the moisture attracted to it by reason of its hygroscopicity results in active decomposition. Air alone is capable of bringing about decomposition of tethelin because tethelin is quite prone to oxidation. Therefore, in dispensing and using tethelin certain precautions must be carefully observed.

The object of this paper is to point out the chemical characteristics of tethelin in so far as they demand the employment of particular precautions in dispensing and using this sensitive substance, and in addition, to point out the manner in which this substance has been employed.

## PHARMACOLOGIC ACTION AND MANNER OF USE.

Three of the lipoids especially concerned in the process of growth are cholesterin, lecithin and tethelin. Cholesterin and lecithin have been extensively studied. We are indebted to Robertson for the researches which have resulted in developing our knowledge of tethelin as a powerful agent in influencing the process of growth in the animal body. It apparently retards growth when administered to animals before the age of adolescence and accelerates growth in the post-adolescent period.<sup>2</sup> It increases the rate of growth of the Flexner-Jobling carcinoma in rats in the same way as the whole anterior lobe tissue.<sup>3</sup>

The effect of tethelin in the process of the repair of tissue was studied by Robertson by experiments on wounded mice. The tethelin was administered hypodermically and showed a stimulating action on tissue repair.<sup>4</sup>

Barney<sup>5</sup> states that "no work has yet been published on the effect of tethelin as an accelerator of repair in cases of delayed union of fractures; but, reasoning from the basis that acromegaly is caused by a hypersecretion of the anterior lobe of the pituitary, it would appear that tethelin would have a very great value in certain cases of delayed union, and may we not anticipate less tedious results on

<sup>2</sup> Robertson, T. B., *Jour. Biolog. Chem.*, 1916, XXIV, 397.

<sup>3</sup> Robertson, T. B., and Theo. C. Burnett, *Jour. Exper. Medicine*, XXIII, 1916, p. 631.

<sup>4</sup> Robertson, T. B., *Jour. Med. Assoc.*, LXVI, 1916, p. 1009.

<sup>5</sup> Barney, E. L., M.S., M.D., *Jour. Lab. and Clin. Med.*, Vol. III, No. 8, May, 1918.



the various forms of skin grafting, also in treating gastric ulcers, and in fact almost all epithelial lesions tending to chronicity?"

Cases of ulcer treated in the Out-Patient Department of the University of California Medical School, by Barney, are reported in his paper from which the above quotation was taken. Applications of gauze, wet with a solution of 100 Mgm. of tethelin in 5 Cc. of sterile distilled water were made and this was followed by dusting the ulcerated surface with 100 Mgm. of powdered tethelin. The tethelin was used in conjunction with the regular surgical procedures indicated in each case. Subcutaneous injections of tethelin were given beneath the ulcer in certain instances or injected along the margin. In other cases lanolin, medicated with tethelin was used. In all of these cases the improvement was sufficiently marked to warrant the opinion that the excellent results might probably be ascribed to the tethelin applications. These results could not be attributed to the regular surgical treatment of the cases for the reason that the improvement was not marked until after the tethelin applications had been made.

Since tethelin is a fatty substance and readily hydrolyzed by alkalis, it is probably partially decomposed in the intestine by the alkaline juices and also probably by the pancreatic lipase. A large part of the tethelin administered by mouth is therefore in all probability wasted.<sup>6</sup>

As a consequence, treatment by mouth is not to be depended upon, except as an adjunct to the hypodermic use of the substance.

The experimental work of C. L. A. Schmidt<sup>7</sup> has shown that tethelin is non-toxic and non-antigenic, hence it should be therapeutically without danger to the patient.

Robertson and Ray<sup>8</sup> found by experiments upon mice that the onset of senescence in tethelin-fed animals was markedly deferred and that the spontaneous origin of carcinoma, which is essentially a disease which accompanies a measure of senescence, suffered more than proportionate delay, as a consequence. Even more marked than the delay in its growth in the incidence of carcinoma was the delay in its growth in the tethelin-fed animals. In inoculated carcinoma, the administration of tethelin caused marked acceleration of the growth.

<sup>6</sup> Robertson, T. B., "Endocrinology," 1917, I, p. 34.

<sup>7</sup> Schmidt, Carl L. S., Ph.D., *Jour. Lab. and Clin. Medicine*, 1917, II, 711.

<sup>8</sup> Robertson, T. B., and L. A. Ray, *Journ. Biolog. Chemistry*, 1919, XXXVII, p. 446.

The belief was later expressed by Robertson and Ray<sup>9</sup> that the direct action of tethelin appeared to consist of retardation of growth, and that the later acceleration is due to compensatory factors which develop in the animal itself in response to the abnormal dosage of the active principle of the anterior lobe of the pituitary body.

They preferred this view for the reason that the compensatory acceleration was more intense when the retarding factor, tethelin, was discontinued after the twelfth week of age of the mice and the eighth week of the administration. Finally they presented two possibilities to explain the effect of tethelin upon the healing of superficial wounds and upon the growth of inoculated carcinoma, namely, that tethelin accelerates the growth of the epithelial tissues and directly or indirectly retards the growth of the other and collectively more bulky tissues, or that tethelin retards the growth of all tissues, but indirectly accelerates the growth of epithelial tissues in situ by disproportionately retarding the growth of other tissues and thus favoring the epithelial tissue in the competition for nutritive materials.

#### PHYSICAL AND CHEMICAL CHARACTERISTICS.

Tethelin is a white or pale cream-colored substance, which is readily powdered. It rapidly absorbs aqueous vapor when exposed to damp air and becomes moist and darkens in color.

A combination of air and moisture results in active decomposition of tethelin, the tethelin becoming damp and dark in color and suffering a lowering of its iodine-absorption power.<sup>10</sup>

When heated, tethelin begins to darken at a temperature lying between 100 and 110° C., and when heated to still higher temperatures, the substance progressively darkens and softens as the temperature rises.

Heat is particularly active in bringing about decomposition of tethelin, particularly in access of air and moisture.<sup>11</sup>

Tethelin is soluble in water to the extent of 5 per cent., forming at that concentration a brown, turbid solution. More dilute solutions are paler in color and 1 per cent. solutions are but slightly opalescent. Aqueous solutions of tethelin have a greasy odor, somewhat resembling brain tissue.

<sup>9</sup> Robertson, T. B., and L. A. Ray, *Journ. Biolog. Chemistry*, 1919, XXXVII, u. 456.

<sup>10</sup> Robertson, T. B., *Jour. Biolog. Chem.*, 1916, XXIV, p. 415.

<sup>11</sup> Robertson, T. B., *Calif. State Jour. Med.*, Dec., 1917.

Aqueous solutions of tethelin are faintly acid in reaction.

Tethelin is soluble in ethyl alcohol and to a less extent in ethyl ether, the solutions in ether being marked by opalescence at high dilutions. It is also soluble in chloroform and in carbon tetrachloride. It is insoluble in a mixture of one part by volume of absolute ethyl alcohol and one and one half parts of dry ether.<sup>12</sup>

When ignited until free from carbon, tethelin yields a few per cent. of ash.

The exact chemical nature and structural formula of tethelin have not as yet been thoroughly established. It partakes of the nature of a lipid. It is capable of being saponified by alkalies and possesses iodine-absorption properties. It contains phosphorus and nitrogen. Part of the nitrogen is in the amino form. The proportion of amino nitrogen is increased after hydrolysis by barium hydroxide. Among the products yielded by hydrolysis with barium hydroxide followed by hydrolysis with dilute sulphuric acid, is inosite. The presence of both phosphorus and inosite in tethelin is of great interest in view of the presence of "phytin" (inosite-hexaphosphoric acid) in the rapidly growing parts of plants and in milk, and its probable importance in connection with the growth of tissues. Tethelin probably contains an iminozoyl group and to this extent may be regarded as being related to the physiologically active substances of the posterior lobe of the pituitary body. It does not, however, possess the characteristic physiological activity of these substances.<sup>13</sup>

#### PRECAUTIONS TO BE OBSERVED IN DISPENSING TETHELIN.

Tethelin in dry form should at all times be preserved in a sealed glass tube in which a vacuum has been created. It is extremely hygroscopic, the moisture of the air being readily absorbed by it and thereby lowering its activity in proportion to the quantity of moisture absorbed.

In addition it is also extremely prone to oxidation upon exposure to air. Robertson advocates the use of vacuum tubes which contain 100 Mgm., since this is the quantity which is generally accepted as being satisfactory for use at one time.

It is most desirable that the whole of the contents of a tube of tethelin be employed when the tube is opened and that, under no

<sup>12</sup> Robertson, T. B., *Jour. Biolog. Chem.*, 1916, XXIV, p. 411.

<sup>13</sup> Robertson, T. B., *Jour. Biolog. Chem.*, 1916, XXIV, pp. 409-421.



circumstances, the residue left after partial use of the contents of a tube be used, if it has been exposed to the air for some time and has become moist and dark in color.

Because of hygroscopicity and proneness to oxidation, tethelin should not be dispensed in capsules or tablet form, without special means being taken to protect the products from air and moisture, except for the most extemporaneous use.

#### THE MANUFACTURE OF STERILE PREPARATIONS OF TETHELIN.

Dry tethelin withstands a temperature of 80° C. without apparent change in physical appearance, but begins to darken between 100 and 110° C. It will thus be evident that this substance is quite sensitive to the degree of heat commonly employed in sterilization. Dry tethelin can be prepared in a final sterile condition only by the exercise of the utmost care in maintaining sterile conditions throughout the process of manufacture and placing the finished product through a thorough sterilizing process under carefully regulated temperature which is not allowed to rise above 80° C. Sterility tests on the final product are absolutely essential in order to obtain positive assurance of its safety for hypodermic use.

Sterilization of tethelin in the dry form should never be attempted at a temperature above 80° C. As supplied in tubes, tethelin is sterile as proven by actual bacteriological tests. If extra sterilization is desired, the most safe and satisfactory method is to place the tube in boiling alcohol, the alcohol being boiled by means of a steam bath or an electric stove, and not over a naked flame.

Heated water as a bath should not be employed for the sterilization of tethelin unless convenient means are available to regulate the temperature of 80° C., since if the temperature is permitted to mount near to the boiling point of water, the substance will soften and darken and become decomposed, to some extent.

Heat is particularly active in bringing about decomposition of tethelin, particularly in access of air and moisture. For this reason, no attempt must be made to sterilize solutions of tethelin by heating them in contact with air. The proper method of preparing sterile solutions of this substance is to add the sterile powdered tethelin directly from its tube to recently sterilized and cooled water contained in a sterile glass vessel. The tethelin dissolves immediately upon slight agitation of the mixture and is then ready to be drawn directly into a sterile hypodermic syringe.

Tethelin normally forms a turbid solution with water, therefore no attempt should be made to filter the solution perfectly clear. Extraneous particles of foreign matter such as fibers, particles of dust, glass, etc., which may accidentally find their way into a solution, while it is in process of preparation, may, of course, be removed by rapid filtration of the solution under perfectly sterile conditions. It is, however, quite unnecessary to labor to attain a perfectly clear filtrate, before use. The same care must be exercised in regard to sterility, in preparing a solution for local use as for hypodermic use. Aqueous solutions of tethelin are faintly acid in reaction. The acidity of tethelin is one of its chemical characteristics and is so slight as to have no corrosive effect whatever upon metallic hypodermic syringes.

Schmidt<sup>14</sup> found that *B. coli* and *B. proteus* could grow in a medium containing 1 per cent. of tethelin and a trace of salt.

A quantity of tethelin in a semi-dry state which was contributing to the growth of *B. Hay* has come under my observation.

The fact that a solution of tethelin is a culture medium for certain bacteria indicates the necessity of employing only freshly sterilized and cooled distilled water in the manufacture of its solutions. The same is true of any other liquid or semi-liquid vehicles as might be employed, such as ointment bases for the manufacture of ointments of tethelin. These bases should be rendered sterile at 100° C., and should be cooled before the tethelin is incorporated.

Tethelin solutions and any extemporaneous preparations of tethelin must be freshly prepared and not kept as stock solutions or preparations. The difficulties of keeping stock solutions and stock preparations of tethelin sterile under the conditions usually obtainable outside of a bacteriological laboratory are quite insurmountable because of the extreme readiness with which certain microorganisms make use of tethelin for their growth.

#### PRECAUTIONS TO BE OBSERVED IN USING TETHELIN.

Tethelin is lipid in nature and as a consequence is subject to hydrolysis in the presence of alkaline substances. For this reason, it is not advisable to employ it in admixture with such more or less alkaline wound dressings as neutral sodium oleate, soaps, sodium phenolate, calamine, zinc oxide, ichthyol, sodium hypochlorite, sodium

<sup>14</sup> Schmidt, Carl L. S., Ph.D., *Jour. Lab. and Clin. Medicine*, 1917, II, p. 717.

borate, sodium bicarbonate, carron oil, etc. It is also not advisable to employ it locally following the use of any of these substances until the wound has been freed from them. Hypodermic use of tethelin is indicated during the period of local use of any of these more or less alkaline substances.

By virtue of its lipoid nature, tethelin possesses considerable iodine-absorption power. For this reason, it is not advisable to employ it in admixture with dusting powders, liquids, ointments or other preparations which contain free iodine or which are capable of liberating free iodine when used on a wound. It also is not advisable to use it locally, following the employment of any of these substances until the wound has been freed from them. The use of tethelin, hypodermically, is indicated during the period that any of these free-iodine-bearing or free-iodine-generating substances are being employed locally.

Tethelin in any form must not be permitted to come into contact with substances possessing oxidizing properties. Some such substances are sodium hypochlorite, potassium permanganate, ferric chloride, peroxides, chlorates, bismuth subnitrate, carron oil, ozonized oils, iodized oils, etc. When such substances are being employed locally, it is advisable to postpone the local use of tethelin until the wound has been freed from them. Hypodermic use of tethelin is indicated during the time over which such oxidizing substances are being employed locally.

#### SUMMARY.

Tethelin is suggested as being the growth-controlling principle of the anterior lobe of the pituitary body.

It has been employed hypodermically in solution form; locally in solution, as a dusting powder and in ointment form and by mouth.

It partakes of the nature of a lipoid.

It is an extremely sensitive substance, even air and moisture causing active decomposition.

Extemporaneous preparations made under the usual pharmaceutical conditions should be employed as soon after manufacture as possible and not stocked.

Tethelin in the dry form and in solution form must not be heated above 80° C.

Tethelin in solution form must not be sterilized by boiling in the air.



Sterile tethelin solution can be prepared by adding sterile tethelin to cooled sterile water.

It is not advisable to employ tethelin in admixture with oxidizing or alkaline substances or substances containing free iodine or which are capable of generating free iodine.

Hypodermic use of tethelin appears to yield the maximum activity of the substance.

Because of the extreme sensitiveness of tethelin to moisture, air, common wound dressings and digestive ferments and because of the exposure to these agents to which tethelin is subjected when employed by mouth or locally in any form, its use locally or by mouth is to be recommended only as an adjunct to its hypodermic use.

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## THE RAW MATERIAL SITUATION.<sup>1</sup>

BY CHRISTIAN BEILSTEIN.

I had the privilege of addressing last year's convention of your association on the same subject your committee has requested me to discuss today—the raw material situation. In the meantime a great deal of water has passed under the bridge, but I confess frankly that if it seemed difficult then to attempt to forecast the immediate future, it is little if any less so now. A year ago the answer to the question, What about the future? was apt to be, Tell me how long the war is going to last and I will tell you what I think will happen after it is over. Well, the war came to an end rather suddenly about six months ago, if we may believe all we are told, but the perplexities of business did not end with it by any means—they merely changed about after the manner of the kaleidoscope; and what lies beyond the mists just ahead is still a matter largely of conjecture. I think however that from our experiences since last fall, we can draw a few conclusions which will be both safe and of some practical value, and one or two of these seem to be directly in point of our subject.

As we all know, one of the conspicuous commercial develop-

ments of the war period was a tremendous and almost universal advance in prices, brought about chiefly by scarcity of materials and increased cost of production and transportation. Many of the products you are constantly using went up to from 5 to 25 times their normal values. Some finally disappeared entirely, while others were kept in limited supply by provisional domestic manufacture, which had become possible only because of the high prices obtainable. The obvious problem which arose out of this condition was whether, upon the ending of the war, this entire fabric of enormously inflated prices would collapse suddenly and at once like a punctured balloon, or whether there was a fairly good chance of a slower and more gradual decline, the one alternative of course spelling terrific losses, and the other an opportunity to make the transition from the one level to the other with reasonable safety. There was a deep-seated fear that the countries of the central powers, having suffered practically not at all from the actual devastation of the war, might by some magic be able to resume manufacturing and shipping their usual products immediately upon the cessation of hostilities. Needless to say, very few men if any, were able to foresee the conditions under which hostilities actually did cease, and no one could have imagined what really took place and is still taking place within those countries. When the crisis came, the signing of the armistice was the signal for a swift and general change of position and attitude by manufacturer, merchant and speculator alike. There was no panic, but the feeling was very much like one. To get rid of high cost stock on hand with minimum loss and to refrain from buying more except from sheer necessity, was instinctively felt to be the thing to do. Business inevitably received a distinct set-back, but there was no collapse. Individual articles went down in price for varying specific reasons. Others on the contrary went up—some logically as had been expected of them; some unexpectedly and for reasons which had not been foreseen. The general average of prices however remains abnormally high, and we now know that it could not have been otherwise and that it cannot be for some time to come. There must of course be a steady and increasing pressure downward on those commodities which are still being produced under what are practically war conditions, or the prices of which are being kept up artificially. But we could not expect to have low prices on goods

which come normally from Russia, Germany or Austria, even assuming we wanted goods from there and could get them. We cannot expect the products of war-shaken France to come out at old prices even when her shattered industries again strike something like their natural stride. The same is true of the other allied countries. It is true of the neutrals or most of them, and it is true finally of ourselves. The whole world is staggering under the burden of a war debt of almost incomprehensible magnitude. Anarchy, strikes, turmoil and terror are rampant practically throughout Europe. Our own country has remained physically almost untouched by the war, while commercially and financially we have prospered enormously. But our very prosperity and the tremendous excess of activity which it engendered have brought us high prices; and the reasons are plain and on the surface. We all know the extraordinary condition of the labor market. We know the plight of the railroads and other public utilities and what it is costing us. We know the governmental strong arm program of maintaining farm products at exorbitantly high price levels and what the consequences must be. We know that gold is substantially at a discount. We know finally that all these things acting and reacting upon each other have to an alarming extent impaired the purchasing power of our money, and this literal cheapening of the dollar naturally and inevitably finds direct expression in high prices. We are taking it for granted that as a matter of course these abnormal conditions will somehow gradually correct themselves, and that ways and means will be found to help along the remedial processes; but it must also be obvious that this will take time and that the period of re-adjustment and re-construction will be much longer than we thought. We can and must all help to shorten this period, and the point I wish to make here is that the way *not* to do our share of this work is to allow ourselves, from fear of the bugaboo of crumbling prices, to sit tight in a mistaken attitude of self-preservation and practically stop doing business simply because the business may not promise to be as profitable as it has been during the past two or three years.

By way of illustration of the fact that instead of a sudden collapse of values we have had only a partial and orderly decline, I have plotted for comparison the prices of 25 representative perfumery raw materials, synthetics and essential oils, which you are



all constantly using. The average price of these 25 materials in 1914 before the war was thought of was \$17.00. By the middle of last year, before the end of the war was clearly foreshadowed, this average price had risen to \$33.50, almost one hundred per cent. At the present time the same 25 materials represent an average of \$28.50, which is to say that they have lost only about a third of the total advance and still average more than 50 per cent. higher than their pre-war level. Such an average price of course means nothing to the individual who paid \$65.00 for methyl anthranilate last year and now sees the price at about \$15.00; but it has some value as a composite of the actual performances of the market.

As to the present position and apparent prospects of individual materials or groups of materials, I shall limit myself to a few brief references. The synthetic situation is now clearing up fairly rapidly, and comparatively few products remain unobtainable. The release from their war status of such chemicals as acetone, toluol and the like, has already been reflected in the materially increased supply and lower prices of such products as the ionones, benzyl compounds, and others. Ability to bring forward heavy accumulations of clove spice from Africa has lowered clove oil fully 50 per cent. and will have a material effect upon the group of aromatics derived from it which include as you know the important carnation bases. The foreign manufacturers of these fine chemicals are of course still struggling with enormous difficulties and it remains to be seen just how complete a recovery they can make without going to Germany for many essentials, as they did before the war; but they can at least now see daylight ahead and I think we may reasonably expect the synthetic line in most if not all of its ramifications to be in fairly good shape and on a practicable price basis before the end of the year.

In the field of natural floral products and essential oils the process of restoration may similarly be expected to make reasonably rapid progress. The industries of southern France and the other Mediterranean producing countries which struggled along so wonderfully during the war period are still handicapped enormously by the want of labor, fuel, transportation, raw materials, containers and what not; but conditions will undoubtedly improve as steadily and satisfactorily as we have any right to expect. Such oils as the geraniums, neroly, lavender, ylang ylang and vetivert continued to

advance after the close of the war chiefly because of real shortage and to some extent because of obstructed distribution owing to transportation troubles. With the coming of another crop they should be easier, but there is at this time little encouragement to expect an early return to anything like pre-war levels. Sandalwood, amyris and patchouly oils also remain abnormally high in keeping with the raw material situation, both as to cost at primary sources and transportation for the great bulk involved. The otto of rose question remains almost as much of a mystery as it was a year ago, but it cannot continue so much longer. Heavy shipments of other products have been permitted to come out of Turkey and Bulgaria and with them have come some dribbles of rose oil which the shippers have doubtless hoped to sell at famine prices. Unless all conjectures have been wrong however, there must soon come a heavy flow of this important material and with it something like practicable values.

Animal musk became so scarce and dear in China that its importation was brought practically to a standstill; but here too we have signs of material improvement and there are shipments on the way from the East at prices which, while far from low, are at least not impossible. Civette was extremely scarce for a time, not because it did not exist, but because the Mediterranean embargo made it impossible to bring shipments through. The supply is now somewhat better and the price did not at any time advance unreasonably. Of ambergris no catch or find of any importance was reported during the past year. The last good sized lot, something over 100 pounds of exceptionally fine quality, came to this market two years ago and you will be interested to know that, notwithstanding the war, it all went to France. The replenishment of the supply in this case is of course a matter of fisherman's luck and at least for the present we shall have to get along without it.

I shall not detain you longer with an extension of this catalogue. The placing of one's finger today on a fact which was elsewhere yesterday and will probably be again removed tomorrow, is of little value except in following that particular fact. What we are concerned with is the general aspect of our question rather than the particular, and I think that we may consider this general aspect fairly presented in the group of average market prices cited, which to my mind indicate that we have probably emerged about one half

from the chaos in which we were last November. We shall most likely be much longer extricating the other half and as to some things I dare say we may never get back where we once were. To sum up the matter I think we are justified in saying that the situation of this industry in respect of its raw materials is broadly about the same as that of the country at large. We have come through the storm without shipwreck, and while we are still wallowing in troubled waters and hampered by the fog of uncertainty, all we need to keep off the rocks is watchfulness, self-confidence and a little more of the same kind of luck we have had.

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## A REVIEW OF THE ADVANCES IN PHARMACY.

BY JOHN K. THUM, PH.M.,

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*Dichloramin-T and Petrolatum Dressing for Burns.*—Dr. Sollmann, of the Western Reserve University School of Medicine, recounts a detailed study of this substance undertaken in the pharmacologic laboratory of the university. Dichloramin-T has the very real advantage of furnishing a continuous supply of the antiseptic agent, the action being continuous for long periods of time and can be applied with the simplest form of dressings. Of course the importance of a substance that will supply continuous antiseptic action over quite a period of time when it is impossible to kill all the bacteria at once can be readily appreciated. Its convenience of application can also be readily appreciated. However, dichloramin-T has some rather glaring disadvantages. The solutions must be prepared with some care, and must be fairly fresh, or else treated for the presence of available chlorine. Application causes considerable smarting and burning. This, though, disappears promptly and can usually be tolerated. It is very prone to irritate the skin after repeated applications.

In most cases these advantages are of little import and can be overlooked. In connection with the treatment of burns, however, limitations manifest themselves that must be reckoned with. The large open surfaces require protection against mechanical irritation and access of air, and dichloramin-T-chlorcosane solution fails in



this particular. It was found that this solution is absorbed by the dressings, which are then glued by the wound secretions, which cause pain and injury when the dressings are removed or changed. It was also noticed that paraffined lace-mesh gauze does not prevent this.

Such results were particularly conspicuous in the case of the very painful and slow healing "mustard gas" (dichlorethylsulphide) burns that came under the doctor's observation. When such burns get to the ulcerative stage, they become so sensitive that they have to be protected by thick petrolatum dressings, especially at night. As such dressings give protection to the bacteria as well as to the tissues, they are particularly undesirable. Infection flourishes and healing is delayed. It was hoped to obviate this either by alternating the antiseptic and protective dressings or by applying a petrolatum dressing to the wound after it had been painted with dichloramin-T-chlorcosane solution (generally of 2 per cent. strength).

Notwithstanding the fact that dichloramin-T is gradually destroyed by ordinary petrolatum it was hoped that the destruction would be so slow that some of the antiseptic would last from the one dressing to the next. This was not realized. This conclusion led to a more detailed investigation of the destruction of dichloramin-T by petrolatum and various other solvents. The result was a special petrolatum medium which was found to be sufficiently compatible with dichloramin-T for surgical purposes, so that it may be applied either mixed directly with the dichloramin-T or as a protective dressing over the dichloramin-T.

Dr. Sollmann calls attention to the fact that liquid and semi-liquid mixtures of petrolatum with active drugs are not subject to the same limitations as is the incorporation of these drugs into solid paraffin. Solid paraffin prevents adequate contact of the mass of the antiseptic with the wound. On the other hand, he says, the layers of liquid and semi-liquid mediums in contact with the wounds are continuously changed, so that good contact is secured.

The rapidity of destruction or deterioration of dichloramin-T in various solvents was estimated by the changes in the "available chlorine," occurring at successive periods in solutions or mixtures containing originally two per cent. of dichloramin-T.

This was done by the method mentioned in "New and Non-official Remedies," 1918, p. 158. To duplicate 5 Mil or 5 Gram

samples of the mixtures to be tested, there were added 5 Mils of glacial acetic acid, 10 Mils of ten per cent. potassium iodide, and sufficient carbon tetrachloride or chloroform to thin the material (usually about 5 Mils); then a few drops of starch test solution, and finally, from a burette, sufficient tenth-normal sodium thiosulphate solution to discharge the color.

Each Mil of tenth-normal sodium thiosulphate solution corresponds to 0.0177 Gram of available chlorine.

The solvents worked with were two samples of chlorosane; two of liquid petrolatum; five of petrolatum; carbon tetrachloride, which gives the most stable solutions; kerosene, which is very destructive, in fact more so than olive oil. Liquid petrolatum solutions show some loss at once, but preserve a fair efficiency for a month. Chlorosane solutions keep practically perfect for three days, and after that are fairly active for a month. Ordinary petrolatums are very destructive for dichloramin-T; in fact the efficiency is destroyed at once. The amount of deterioration is the same regardless of the color impurities in the petrolatum.

The conclusions of this laboratory investigation of dichloramin-T show that an ointment of three parts of surgical paraffin and seven of liquid petrolatum has relatively little destructive action on dichloramin-T and can be used as a protective dressing on wounds (burns) treated with dichloramin-T-chlorcosane solutions, and even as a basis for a dichloramin-T ointment.

Ordinary petrolatum, irrespective of its color, is very destructive of dichloramin-T, and cannot be used effectively with it.

Liquid petroleum can be used in emergencies as a vehicle for dichloramin-T, although it is inferior to chlorcosane.

Solutions of dichloramin-T in carbon tetrachloride are very stable, while those in kerosene or in olive oil spoil very rapidly.—*Jour. A. M. A.*, April 5, 1919.

*Cinchona Research in Java.*—It may not be generally known that a cinchona experiment station exists in Java. This station was founded in 1911, and though it has issued a few bulletins, it has not published an annual report until this year when the reports for 1916 and 1917 were issued together. The station has for its object the study and investigation of this important drug-plant in all its phases, and to be in a place to give advice on agricultural, botanical, chemical, and entomological matters to those who are interested in the

development of this industry. Analyses of bark are made for which a reasonable charge is made. A botanical research has been undertaken on the morphology of flower and fruit formations in cinchona, which is expected to bring forth results of considerable value in connection with the production of hybrids.

The effect of humidity on the causation of disease in cinchona, is receiving some attention, as is also the question of the loss of seed in seed-beds. This study has been stimulated by the many complaints of the quality of seed supplied by the authorities to those conducting cinchona plantations. These losses were due to attacks by mites. In questions of this sort the services of an entomologist are needed. The effect of the temperature of drying on the alkaloidal content of the bark is a very important one and is receiving attention.

It is of interest to know that cinchona plants are being introduced into the Philippine Islands from India. A missionary institution at Sagada, Island of Luzon, is the pioneer in this attempt. The cultivation of cinchona has never been attempted before in the Philippines.—*Chemist and Druggist*, 91 (1919), p. 45 and 70.

*Acetyl-Amido-Ethoxy Benzene*.—To the foregoing the coined name pertonal has been attached, which no doubt will make it popular with the laity and tend to encourage self-medication in the same manner that the giving of the euphonious title "aspirin" to acid acetylsalicylic, has proven. The action of this combination has been studied and compared to acetphenetidin. It has about one half the toxicity of the latter and as an antipyretic it produces similar effects in doses about double those of acetphenetidin. While acetphenetidin has a direct depressant action on the heart, this organ is actually stimulated by pertonal. Against an antipyretic ratio of two parts of pertonal to one part of acetphenetidin, the corresponding ratio for narcotic action is approximately 15 to 1. It can be said that in general the action of pertonal is less abrupt and more prolonged than that of acetphenetidin. It was shown that both drugs are excreted mainly in the urine in the form of p. amidophenol and phenetidin. It seems that a larger amount of phenetidin and a correspondingly smaller amount of p. amidophenol is set free in the tissues by pertonal than by acetphenetidin. No evidence of the formation of methemoglobin has been found after the intake of pertonal, although this change is often noticed after the intake of



acetphenetidin. Although it was particularly sought for, no evidence of oxalic acid formation after the intake of pertonal was found. The investigator, Dr. Cow, advises a range of therapeutic dose of from 0.6 to 1.2; he also suggests that the dose need not be repeated so frequently as the dose of acetphenetidin.—*Jour. Pharmacology and Experimental Therapeutics*, Baltimore, 12 (1919) 343, through *Jour. A. M. A.*, April 5, 1919.

*Russian Rhubarb*.—From an investigation of rhubarb cultivated in Russia the investigator is of the opinion that the oxymethyl-anthraquinone is the same as that found in the Chinese drug. Furthermore, he found that the Russian drug contains more emodin, more oxymethylanthraquinones and more anthraglucosides. The investigator, whose name is Semmel, also found that large quantities of the last two substances appear to be formed during the drying of the drug.—*Archiv. d. Pharm.*, through the *Pharmaceutical Journal*, March 8, 1919.

*The Cultivation of Rhubarb and Liquorice in Switzerland*.—Attention is called to localities in Switzerland where the cultivation of these well-known drugs would be attended with success. In mentioning this, Tschirch calls attention to *Rheum tanguticum*, which probably yields the best rhubarb, is a mountain plant, and says that it is fair to assume that it would probably flourish in open woods at an elevation of from 2,000 to 3,000 meters. From a well-grown plant it would be possible to take every year from twenty to thirty or more lateral rhizomes for cultivation, in this manner a few plants grown in an experimental garden would provide a large number of new plants each year. The delta of the Maggia, on the Lago Maggiore, near Locarno, would be an ideal spot for the cultivation of *Glycyrrhiza glabra*, which flourishes best in wide valleys on the banks of rivers that often overflow. As at the present time this region is uncultivated no obstacles would stand in the way of its use for this purpose. It has been estimated that if the cultivation were begun now, the canton of Ticino could in ten years' time supply the whole world with liquorice, for the cultivation of this plant is quite simple and the multiplication of the plants is very rapid.—*Schweiz. Apoth. Ztg.*, vol. 56, p. 257, through the *Pharmaceutical Journal*, March 8, 1919.

*Food Reserves in Woody Plants*.—Investigations by Sinnott on the distribution of starch and fat in a large number of woody

plants at various seasons leads him to believe that during winter starch is commonest in regions remote from centers of production, and in cells with thick, well-lignified, small-pitted walls, and that fat is most abundant in and near the phloëm, close to the vessels, and in cells with thin or unlignified walls or large pits. He says that where the movement of liquids is slow, starch predominates, and where such movement is easy, starch disappears at the beginning of the winter, and fat is produced. He believes that this manner of food reserve may be due to differences in the water content of the storage cells giving a modification of enzyme action or to differences in the case with which enzymes have effective access to the storage cells.—*Botan. Gazette*, vol. 66, p. 162, through the *Pharmaceutical Journal*, March 8, 1919.

*Comfrey Extract for Boils*.—Dr. Brunier states that a soft extract of comfrey root in his hands has been found to be an excellent remedy for the treatment of those distressing things, boils. He gives it in doses of 0.6 Gram three times a day. At the end of from twenty-four to forty-eight hours the inflammation lessens, the pain disappears, and on the third or fourth day the pus is discharged. If there happen to be several boils the more advanced ones go through the process just described and the others are absorbed; no new ones are developed.—*Presse Médicale*, May, 1918, through the *Pharmaceutical Journal*, March 8, 1919.

*Castor Oil as a Dressing for Wounds*.—Dr. Revillet in the *Lyon Médicale, Répertoire de Pharmacie*, states that in his experience he has found this oil to be an excellent basis as a dressing for wounds. He claims that it is non-irritant, non-drying, does not adhere to the tissues, penetrates well, and mixes with alcohol and essential oils. He found the following mixture ideal for this purpose:

Oil of thyme .....	45.0 Mils.
Oil of lavender .....	45.0 Mils.
Oil of eucalyptus .....	5.0 Mils.
Castor oil, to make .....	1,000.0 Mils.

This mixture may be applied direct to the wound or used to impregnate the gauze compresses or muslin bandages.—*The Pharmaceutical Journal*, March 8, 1919.

*The Pharmacologic Action of Allocaine S.*—This drug and Allocaine A. are synthetics made by Nagai by introducing into mydriatine

mono-ethyl and di-ethyl and benzoyl groups. The pharmacologic action of Allocaine S. has been studied by Kubota, of Mukden, Japan. He observed that it causes paralysis in frogs and convulsions in rabbits, acting on the central nervous system. The lethal dose, he says, is smaller than that of either cocaine and procaine, when injected subcutaneously. It causes a local paralysis of sensory nerve endings and nerve fibers, and its anesthetic power is stronger than procaine and weaker than cocaine. Kubota noticed that Allocaine S. has a twofold action on blood vessels: a primary dilation and a secondary constriction, and in warm-blooded animals the former action, and in cold-blooded the latter appears more pronounced. A slight local irritation is caused by subcutaneous injections. Large doses of the drug paralyzes the heart, acting on the motor apparatus and conductive system, and causes in frogs a paralysis of respiration and in rabbits a stimulation of it; this action seems to be the central character. It also has an influence on the blood pressure. The substance causes a primary fall of pressure which is followed by a rise above the normal. It also inhibits the growth of both streptococci and staphylococci which is a great advantage. The investigator states that Allocaine S. is a good local anesthetic in many respects, but on the other hand it has also some unfavorable qualities. However, its use may prove to be rather limited on account of its acid solutions and its tendency to precipitation by the tissue fluids. Notwithstanding this Allocaine S. has been used in several hundred cases of operations with success.—*Jour. of Pharmacology and Experimental Therapeutics*, Baltimore 12 (1919), 343, through *Jour. A. M. A.*, April 5, 1919.

*Gelatin Tannate*.—According to E. Choay, *J. Pharm. Chim.*, 16 (1917), 137, the preparation of tannate of gelatin offers no obstacles in its manufacture and really is a reliable substitute for certain organic tannin compounds, such as tannalbin and tannigen, which were at one time rather popular with physicians. Ten Grams of a good gelatin are dissolved in the greater part of one liter of distilled water; twelve Grams of tannic acid are dissolved in the remainder. The tannin solution is now poured in a thin stream into the cold gelatin solution with constant stirring. The precipitate is allowed to settle and the supernatant liquor treated with a little more of either solution to determine if either is in excess. If so, sufficient of the required solution is added to bring about complete precipitation. A cloudy mixture indicates excess of gelatin. The super-



natant liquor is then decanted, the precipitate drained and rapidly dried at a moderate temperature. Gelatin tannate, prepared in this manner, is a white odorless nearly tasteless powder; almost insoluble in water, dissolved by alkalies, and insoluble in acids. It has proven to be a good intestinal astringent, being less irritant to the stomach than tannin and most other tannates. For an adult the dose is 0.5 Gm. given from four to eight times each day. Children can be given from two to three decigrams four or five times each day.—*The Pharm. Jour.*, 102 (1919), 172.

*Peppermint Cultivation in Holland.*—It is claimed that the experimental cultivation of this most popular household remedy is being attended with promising results. Two lots were found to contain 0.70 and 0.95 per cent. of oil respectively. Taste and odor were deemed excellent. A chemical investigation revealed the following: Refractive index (20° C.), 1.4621 and 1.4615; optical rotation, —29°.2 and —29°; specific gravity, 0.907 and 0.905; ester value, 23.7 and 21; combined menthol, 61 and 63.4 per cent. It is hoped to repeat these experiments next year on a larger scale.—*Pharm. Weekbl.*, 56 (1919), 41, through *The Pharm. Jour.*, 102 (1919), 172.

## PHARMACOPŒIAL NOMENCLATURE.<sup>1</sup>

Prior to the outbreak of the war the necessity of establishing international standards for potent drugs was realized, and in the course of time recognized by all pharmacopœias. But while provisions were made for standardizing the strength of certain preparations nothing was done towards establishing uniformity in nomenclature, either in the Latin titles adopted by different pharmacopœias, or indeed in the names of similar preparations. Thus, at present we have the following official varieties in Latin nomenclature for the same substance: Hydrargyri subchloridum, hydrargyri chloridum mite, hydrargyrum monochloratum, chloretum hydrargyrosus, hydrargyrum chloratum. This lack of uniformity in nomenclature almost led to a Belgian pharmacist being shot, under the following circumstances. A German doctor doing duty at Fort Malonne sent down to the military hospital in Namur a collective

<sup>1</sup> Reprinted from *The Chemist and Druggist*, May, 1919.

prescription for medicines urgently required. In those days the Belgian pharmacists attended to this work, and they found that in addition to carbolic acid, iodoform, formaldehyde, gauze and cotton wool, the following requirement figured on the prescription: "Hydrargyrum chloratum 50 Ag, 10 Stück." The pharmacist who made up the prescription took this to indicate corrosive sublimate, in the first place, as all the articles enumerated were for the treatment of wounds, and, secondly, because calomel, in Belgium, is not prescribed in tablet form. To make quite sure, he consulted some colleagues, and then put up the corrosive sublimate tablets in an octagonal brown bottle, with the words: "Usage Extérieure," "Uitwendig Gebruik," printed in the glass, and on the label he wrote: "Hydrargyrum chloratum—sublimé corrosif," adding a label with a skull and cross bones, and another with the words: "Poison, Vergift." In spite of all these precautions the hospital attendant, seeing the name "Hydrargyrum chloratum," which to him meant calomel, administered a tablet to a patient, with the result that he was poisoned. M. V. Dulière, the chief inspector of Belgian pharmacies, who relates this incident in the *Journal de Pharmacie de Belgique* (No. 13, 1919), says that the pharmacist had to appear before a court-martial on the charge of attempting to cause the death of German citizens. The German authorities, happily, consulted M. Dulière, whose explanations regarding the differences in nomenclature, the special circumstances of the case, and also the precautions taken by the pharmacist in putting up the dangerous drug, convinced the examining officer, and the accusation against the Belgian pharmacist was dropped. M. Dulière mentions this incident to draw attention to the dangers arising from the present variations in nomenclature.

## A SKETCH OF DR. LYMAN SPALDING.<sup>1</sup>

BY HENRY M. HURD, M.D.

Dr. Lyman Spalding was born at Cornish, N. H., in 1775. His early education was obtained at the Charlestown Academy, and later he was a student in the office of Dr. Nathan Smith, the eminent founder of medical schools, and the first of the name of the Smiths who later became distinguished in New England and Maryland. He afterwards visited the Harvard Medical School in 1794 and attended two courses of lectures there, but did not receive his degree of M.D. until 1797. He returned to Cornish, N. H., the residence of Dr. Smith, and took charge of his practice during the latter's absence in Europe. He subsequently taught chemistry and materia medica with Dr. Smith at the newly established medical school at Dartmouth College, N. H. He also became demonstrator of anatomy.

He soon removed to Walpole, N. H., where he practised for a few months also. His residence there is mainly interesting because of the fact that he purchased a set of Perkins Tractors, then much used and highly praised for the treatment of diseases. These tractors were sold for \$20, with the exclusive right to use them in practice both in this country and in Europe. It was one of the common medical frauds which are perpetrated on all nations about once in so often.

Dr. Spalding removed to Portsmouth, N. H., in 1797, and there had a successful career. He became a contract army surgeon, and had so much to do that he relinquished his connection with Dartmouth College. He was a diligent student, and active in all matters

<sup>1</sup> Read before The Johns Hopkins Hospital Historical Club, February 10, 1919. Reprinted from *Johns Hopkins Hospital Bulletin*, May, 1919.

*Editorial Comment.*—In the past, as from time to time we read the "Historical Introduction" to the Pharmacopœia of the United States, the desire to know more about the history of Dr. Lyman Spalding, who in the initial paragraphs, is given credit for originating the project for the formation of a National Pharmacopœia, became stronger with each reading. This desire has been gratified by the publication recently of the "Life of Dr. Spalding" prepared by his grandson, Dr. J. Alfred Spalden. The facts presented in this sketch are taken from this memoir and are presented in such an interesting way that we are of the opinion that the reprinting thereof will be appreciated by many pharmacists.



connected with medical coöperation. He established a medical society, an anatomical museum, and originated and distributed so-called "bills of mortality," giving the causes of death of persons who died in Portsmouth from the years 1800-1813. He also essayed the growing of opium and lettuce in his garden for medicinal purposes.

In the "Life of Dr. Lyman Spalding" several interesting chapters are given on the introduction of vaccination into this country. Dr. Spalding, who was living at Portsmouth, wrote to Dr. Waterhouse, of Cambridge, who had received the Kine Pox from Jenner in England and seems to have had the monopoly of the introduction of vaccination into this country. Waterhouse was undoubtedly a man of ability and energy, but probably lacked money and felt the need of exploiting the new discovery for his own benefit. He, accordingly, writes to Dr. Spalding, in reply to his letter, asking for one quarter of the amount received from Dr. Spalding's vaccinations during the succeeding fourteen months, insists that "the small sum of five dollars" be charged for each vaccination, and guarantees that the exclusive privilege will be granted upon these terms. He also makes careful mention of the fact that he has Jenner's matter direct from England. A long correspondence took place between Spalding and Waterhouse. Both parties seem to have been anxious to make money from the introduction of vaccination, but Waterhouse appears in the most unfavorable light. After acceding to Spalding's proposition that he have exclusive control of vaccination in Portsmouth, he shows great anxiety that he, Spalding, should associate with him a Dr. Cutter and, later, Dr. Cutters' son, on the ground that the activity of these men would increase the number of vaccinations and thereby increase the profits to be derived from the exclusive privilege of managing them. In one letter Spalding asks for the privilege of twelve months, and later suggests that he will pay 10 per cent. of all the sums which he receives for vaccination until such time as vaccination becomes public property. All that he received from Dr. Waterhouse seems to have been the exclusive privilege of vaccinating persons within the limits of Portsmouth, and a small piece of thread which had been dipped in the vaccine lymph. Later it seems that Spalding was to pay \$150 for this piece of thread, and a certain proportion of the money which he received for the vaccina-

tions. Owing to the fact that it soon became apparent that one patient could be vaccinated directly from the arm of another, the exclusive privilege of using the vaccine lymph was soon broken up.

This destruction of the monopoly was undoubtedly much hastened by the unsatisfactory character of the vaccination when the thread impregnated with lymph was used, and the great inferiority of this method to the method of vaccinating from arm to arm. The physicians had many failures. It is also interesting to note that Dr. Spalding, on two separate occasions, made observations upon patients who had been vaccinated and afterwards placed in smallpox hospitals, and freely exposed to the disease for a number of days without acquiring smallpox. Spalding also received a letter from Edward Jenner, the discoverer of vaccination, and subsequently a specimen of vaccine lymph directly from him.

Spalding issued at Portsmouth during the following twelve years bills of mortality—so-called—beginning in the year 1801. Copies of these bills were sent to John Adams, then President of the United States, and subsequently to Thomas Jefferson, Benjamin Waterhouse and Benjamin Rush. Waterhouse, with his usual critical spirit, made reply in the following letter:

CAMBRIDGE, March 18, 1802.

*Dear Sir:* Your letter of the 11th inst. came duly to hand and I have endeavored to comply with your request, so far as to send you some matter on the point of a quill. As to the thread, it is full a month old, but was from a very perfect case and has been kept in a proper degree of temperature ever since. I am now so in the habit of taking the vaccine fluid from arm to arm, that I am not so constant in preserving it on the thread or otherwise. Considerable attention and patience are required in the first use of an old thread. It ought always to be moistened with the vapor of hot water.

You mention my not having answered your last letter. I have received no letter from you since you wrote to me in answer to one of mine. I received a printed bill of mortality, 5 or 6 weeks ago, but no written line whatever with it and I have no letter from you for 4, 5 or perhaps 6 months past.

I have just received "Observations on the Cow Pox" from Dr. Lettsom. I shall probably publish a second pamphlet in a month or so, being practical observations, etc. In the meantime I sent a few to the Medical "Repository" for their next number.

I am glad to find that you attend to the occurrences of Mortality. Excuse me for making a few remarks on the one you were so obliging to send to me. 1. Did ΑΡΗΤΗΛΕ kill the infant, or was it a symptom of another disorder, or in other words: was it sympathetic or IDIOPATHIC?

2dly. We very rarely see consumption in patients above 50 years of age,

more rarely above sixty and very rarely indeed at 70. There is a chronic cough and emaciation, and great expectoration in old people, but it is not the true Phthisis Pulmonalis.

3dly. Is not DEBAUCHERY rather a VAGUE term for a general Head? Does it mean Drunkenness exclusively?

4thly. I never yet saw a very young child with Epilepsy. There is a wide space indeed, between the convulsions of infants, and that truly wonderful disease, EPILEPSY.

5thly. Mortification: Was it in the bowels or the feet? As they are widely different in their cause. See Pott in the LATTEr.

6thly. Death from SCROFULA is very uncommon. It predisposes to fatal diseases.

7thly. PAREGORIC: Does it mean that the Child was poisoned by that composition? If so, had it not better been by Opium as Paregoric means a Mitigator?

You will excuse these hasty observations that occurred on the perusal. They have not originated from a disposition to criticise but from a desire to have them free from every exception.

Yours Steadily,

B. WATERHOUSE.

In 1802 Spalding invented a galvanic battery, which gave rise to considerable correspondence, and which unquestionably was used extensively among his brother physicians. He had letters asking how to make similar batteries and also their exact therapeutic uses. He further devised a process for manufacturing oxygen for inhalation, and later invented a soda water fountain, which seems to have been quite extensively used. As he neglected to protect his invention by patents, as it appears in his biography some years later, patents were secured by other persons, and he was forbidden to use it without paying a royalty for his own invention. He was an active writer, especially upon anatomical and surgical subjects. His practice also extended in surgical lines, and he performed operations for hernia, extraction of cataract and removal of necrosed bone. He continued his interest in vaccination, and received a second letter from Jenner, who acknowledged the reception of some interesting details concerning vaccination and the bills of mortality, for which he thanked him. In Jenner's letter an interesting detail is given concerning the good effect of vaccination in controlling cases of smallpox in Vienna. Prior to vaccination the annual average of such cases was 800. Four years subsequent to the introduction of vaccination, but two cases of smallpox occurred in the city.



Dr. Spalding seems to have had a remarkable facility for friendship, and made warm friends in many parts of the country. One of his friends and subsequent correspondents was Bishop Philander Chase, a boyhood acquaintance, who subsequently became Bishop of Ohio, and later of Illinois and founder of Kenyon and Jubilee Colleges. Dr. Luther Jewett was another friend, a Vermont worthy who had excelled in the practice of medicine, the practice of law, the gospel ministry and the editorship of an influential newspaper; four distinct branches of effort, in each of which he achieved marked success. He was also a warm friend of Dr. John C. Warren, of Boston; Dr. Alexander Ramsay, the famous anatomist from Scotland, and Dr. George Shattuck; of Boston. He wrote letters to John Bell, the distinguished Edinburgh surgeon, and also to Charles Bell, and as his thoughts turned very much to medicine abroad, he made every effort to get an opportunity to visit England and the continent to better fit himself to teach medicine. He sent a petition to the Secretary of State of the United States Government, asking that he be made a special messenger to carry dispatches to France, and received a courteous message to the effect that the services of no such messengers were needed at that time. He visited Philadelphia in order to fit himself better for his profession, and there saw the eminent Dr. Physick, and Drs. Wistar, Rush, Shippen and Barton. He writes that the school in Philadelphia had 350 medical students and later, when in New York, he contrasts the popularity of Philadelphia and the large number of students with the fact that New York had only about 100 medical students.

There is an interesting chapter in Spalding's life which has been detailed at considerable length by his biographer and deserves mention. In 1809 he became connected with the Fairfield Academy, located at Fairfield, about ten miles from Little Falls, N. Y. Fairfield Academy was one of a chain of academies which had been established to promote education in the state under the charge of the board of regents. The great demand for medical men to provide for the needs of an ever increasing emigration to the west at this time gave rise to many medical schools. In addition to the New England schools founded by Dr. Nathan Smith, there were schools at Pittsfield, Mass., and Castleton, Vt., in addition to Harvard and the schools in Philadelphia and New York. He was appointed

lecturer at Fairfield Academy in 1809, and lectured there for several years. The journey to Fairfield from Boston was a matter of three days and nights. He was made lecturer on chemistry and surgery during his first appointment, while Dr. George C. Shattuck, of Harvard, was made lecturer on medicine. The courses seem to have been not simultaneous, but tandem, as it were, Dr. Spalding lecturing on chemistry and surgery for six weeks, and being followed by Dr. Shattuck, who lectured for the same period on medicine, this making a term of three months. The success of the school was so great that it became necessary to erect a new building, and permission was asked of the legislature to establish a lottery to raise \$5,000. Lotteries, it may be remarked, were at this time a popular method of raising money for educational and religious purposes. The Washington Monument in Baltimore was started by a lottery, as also the University of Maryland, the First Presbyterian Church and St. Paul's Church. Many details are given in the biography of Spalding in reference to the lottery plan, and new light is thrown upon it by the suggestion in one of the letters that, if the legislature granted the authority, the privilege of the lottery might be disposed of to some other parties at a discount. The success of the school at Fairfield became so great as to excite the cupidity of persons who were interested in the development of Hamilton Academy, at Clinton, N. Y., into Hamilton College, and an effort to establish a similar medical school at Hamilton. The agitation finally brought an appropriation of \$100,000 to Hamilton Academy, and it became Hamilton College, while Fairfield was obliged to be satisfied with receiving \$10,000 for the construction of a building and a charter giving the privilege to grant degrees, and thus to become an established medical school.

The following letter, sent by Dr. Spalding to Dr. George Shattuck, of Boston, gives a very interesting idea of his conception of the influence of medical teaching, and its benefit to the medical teacher:

*Dear Sir:* I can only say that I regret exceedingly the opinion of yourself and friends, that your avocations will not suffer you to visit Fairfield once more. I acknowledge that, at present, the compensation is not adequate to the output and the loss of business, but, Sir, I do really believe that this school may be made second to none but Philadelphia. If not, I will join with you in resignation. What effect has the Professorship already had on

you? It has compelled you to pay close attention to your profession, to pass the whole of Cullen's "Nosology" in review, before you annually, and thereby qualifying you for the practice of your profession more than any other way in which you could have spent your time. It is the high road to fame, and usefulness. I know that my sacrifices have been great. I know that yours must be. But, show me the man who has risen to be a Prince of Physicians, while slumbering on the couch of idleness.

Soon after I came to Portsmouth, I resigned my office of Professor of Chemistry in Dartmouth, no doubt from the same motives that now influence you, with this addition, that my lectures there had to continue three months. I soon found myself slumbering on my oars and relaxing my pursuits. In fact, so far from improving, I hardly kept pace with the others. A kind of indifference for science pervaded me: Indignant I aroused, I went to Hanover to see Ramsay, I went to Philadelphia, and I planned a voyage to Europe. This change, Sir, I consider the most happy circumstance in my whole Professional career.

Admit that you resign your office. Man is an indolent animal. What inducement have you then, to labor incessantly? None! Your reputation is as high as that of your contemporaries. Then, wrapped in the lap of affluence and ease, you will slumber and sleep till old age creeps upon you, when you will find yourself outstripped in the race of usefulness and fame, your opinions so antiquated as to be regarded not, and yourself a mere old Granny!

Look at the Princes, or rather, Fathers of Physic. Who have they been or who are they now? So far as my memory serves me; Teachers of Physic. Boerhaave, Cullen, Desault. Look at Rush, Warren and Smith. What has put them at the head of the profession? Nothing but their being compelled to labor, and annually to review their profession, and incorporate with their old stock all the new improvements. Show me a man in private practice who does this, annually. He is not to be found. But, your friends say that you can do this, yet stay at home. I acknowledge this, but tell me honorably, Will you do it? No, Sir, you have no inducement. For a man to be pre-eminently great, there must be a great occasion. What made Washington Great? Opportunity. You are now on the same high road to reputation that every Prince of Physicians has travelled. If you turn aside, you are lost forever. These in conjunction with those in my last letter are the reasons which ought to influence you. You can have no doubt of my wishes on the subject. The time for the commencement of the lectures is so near at hand, that no successor can be appointed in season for the next course. I therefore beseech you, on my account, if neither honor nor fame will move you, to deliver This One Course and I will consent to any arrangement that you may then choose to make. If nothing farther, as a mere matter of policy I wish you to withhold your resignation till the meeting of the Trustees of the New Medical College and let us see what they will do for us.

Dr. Mann I knew had been appointed a Hospital Surgeon but I did not know that he had been made Surgeon General. He must be with the Army



by this time and cannot be prepared for the ensuing course. I have no objection to this man, but must for want of room decline saying anything about your successor until I hear from you again. Your friend,

LYMAN SPALDING.

Shattuck, after serving two terms as professor of medicine, relinquished the position, but Spalding, in 1813, was made president of the Fairfield College, and filled most of the chairs in 1814-1815 and 1816. The number of students seems to have varied between fifty and seventy. Spalding seems to have done very faithful, conscientious work, for which he received somewhat irregular pay, and often more pay in promises than in actual money. The school remained in active operation until 1839, when it went to pieces in consequence of squabbles among the faculties as to the division of fees from medical students. The fees seem to have been very small.

In 1814, Spalding went to New York to reside, and had an office on Broadway, for which he was paying about \$200 per year. His fees from his patients during the first year amounted to a little more than \$1,000. At this time, Spalding seems to have attempted to write a book entitled the "Institutes of Medicine" which, as far as I can learn, was never published in book form, but was circulated in pamphlets, each chapter furnishing a pamphlet. It was praised by Shattuck and Waterhouse, and the reception of a sample pamphlet was certainly acknowledged even by Dr. Caldwell, but the book seems to have made little impression.

The following letter is from Governor Plumer, of New Hampshire, a friend of Spalding's:

EPPING, N. H., Oct. 24, 1818.

*Dear Sir:* This week I received your letter with your "Reflections on Fever," and Report of the Trustees of the Free Schools, for which you will please accept my grateful acknowledgments. I have read your pamphlet with attention and pleasure, but it is on a subject with which I am not sufficiently acquainted to decide with precision. You know the low state of the Faculty in New Hampshire. We have scarcely any who write on the subject of medicine, and of the great body of our country physicians but few who have any books, to read those few that they have, or to investigate the complex and intricate subjects of their profession. These facts have long induced me to believe that, in many cases, the patient has more to apprehend from the ignorance of the physician than from the disease and that it is safer to trust to nature for a cure than to rely on the prescriptions of those whose knowledge is limited to a few hard technical terms. With us the Gentlemen

of the Faculty have made less progress than those of law and divinity: the latter, indeed, have much to do before they can attain real eminence.

In your profession I have long considered it a desideratum to have an able but simple work, accurately describing the nature and functions of the several parts of man in a state of health, the effect or changes diseases produce on each of those parts and of the remedies for those diseases.

I would purchase and read such a work with pleasure, and that pleasure would be enhanced if it was simple, plain and free, so far as the nature of the subject would admit, from abstruse technical terms, and of attachment to existing theories. Mystery is the enemy of improvement, and it is better suited to prolong the reign of ignorance and of error than to promote that of truth and science. And, the knowledge of things is vastly more important than that of words.

I really wish we had an accurate Journal kept in different sections of our Country of the actual state of the weather, the crops, the general diet and regimen of our citizens, the diseases most prevalent in each, their type, character and mode of treatment, etc., so as to exhibit the means by which health was preserved and lost and how far they depended on climate and modes of living. Such a Society, I think, might be formed of Gentlemen living in various parts of our Country, with little expense and from whose reports much information could be obtained which would be useful to all, and particularly to Medical Characters. I would freely contribute to such an establishment.

But, I am wandering from the object of this letter, which was to thank you for your Pamphlets and to say, that if you or the Historical Society of N. Y., should need any of the few pamphlets we publish here, it will afford me pleasure to procure and transmit them. I remain with much esteem and respect,

Yours, etc.,

WILLIAM PLUMER.

About 1817 Spalding began to agitate the preparation of a national pharmacopœia, notwithstanding the fact that several local pharmacopœias already existed, the most extensive and authoritative one being that of Massachusetts. His motive in urging a national pharmacopœia was due to his desire to secure uniformity, and also to discard local remedies which seem to have been used in different parts of the United States without any sufficient scientific authority. As an example of such local favorites may be mentioned scutellaria or skullcap as a remedy for hydrophobia. It was shown by Spalding that the authority for the use of this remedy was wellnigh universal. Numerous cures through its employment were reported, and in the literature its claims were overwhelming. We now know that it is worthless, and its elimination from the pharmacopœia was

promptly made. The plan proposed by Spalding for the preparation of the pharmacopœia was an excellent one, and has practically been followed for the last one hundred years.

The pharmacopœia was originated in a paper by Dr. Spalding, read before the medical society in the city of New York, in which he pointed out the difficulties attendant upon the present lack of uniformity in the preparation of drugs in the different states. As a result of the discussion which followed the reading of his paper, a committee was appointed, of which Dr. Spalding was chairman, to suggest measures for the preparation of a national pharmacopœia. The country was divided into four districts, known as the northern, middle, southern and western. Through the medical societies of these regions, delegates were chosen to meet at some central point in the district to discuss matters pertaining to the drugs to go into the pharmacopœia, and to elect two delegates, each to go to Washington later to prepare the book for publication. The only two district conventions were those of New England, at Boston, and of the Middle States at Philadelphia, which met on June 1, 1819. The meeting in Philadelphia, although attended only by delegates from the middle district, had done valuable work in the discussion of remedies and methods. The delegates chosen at the two district meetings met in a general convention in Washington on January 1, 1820, Dr. Spalding being one of the delegates. The two rough drafts from the district meetings were examined and discussed, and the preparation of the pharmacopœia was outlined and plans made for its completion and adoption. A committee of publication was chosen, with Dr. Spalding as chairman, which met in New York in June, 1820. The Pharmacopœia was printed in English and Latin, and was immediately adopted as authoritative throughout the country.

About the same time Dr. Spalding also had, in addition to the pharmacopœia, a plan for the establishment of what he termed a medical police to have charge of all sanitary matters. The latter scheme, however, seems to have faded from public sight.

Dr. Spalding did not live long after the publication of the pharmacopœia. In 1821, while walking in the city of New York, he was struck down by some building material which fell upon his head, and rendered him unconscious. Although he recovered apparently, he never enjoyed good health, and gradually went into a



state of physical and mental decline. He gave up practice, sent his family to New England, and later rejoined them there. He died on October 21, 1821, a few days after he reached them.

It is evident that he was a man of unusual ability, being industrious, efficient, and with large powers of initiative. Imperfectly educated as he was, he had made himself an excellent physician, a remarkable surgeon and anatomist, an interesting and inspiring medical teacher, and a member of the profession full of enthusiasm for its advancement and perfection. He was denied the great desire of his life, the privilege of studying abroad, and doubtless had he been able to do so, and had returned to America with the new ideas, his subsequent labors might have resulted in great additions to the medical knowledge and resources of the country. The story of his life is a most inspiring one.

*Note.*—Since the above sketch was written and presented to the Historical Club, Dr. Kelly has placed in my hands a copy of the first edition of the Pharmacopœia of the United States of America. It bears the following title page:

The  
PHARMACOPOEIA  
of the  
UNITED STATES OF AMERICA.

1820.

By the

Authority of the Medical Societies and Colleges.

BOSTON

Printed by Wells and Lilly.

For Charles Ewer, No. 51, Cornhill.

.....  
Dec. 1820.

It is bound in leather and is in excellent state of preservation. The name on the fly leaf cannot be deciphered definitely. It is in pencil and is dim in places. The inscription seems to be James Burbeck, 1827. It has undoubtedly belonged to a druggist or apothecary as it contains many recipes neatly interleaved in various portions of the book. There are also prescriptions for various diseases. The book contains an interesting historical introduction explaining the object of the preparation of the National Pharmacopœia.

There is also a preface which gives full details as to the movements which led up to the preparation of the work. In the list of delegates originally selected to attend district conventions to prepare lists of medicines and to select local committees are to be found names eminent in the profession one hundred years ago, many of whom figured in medical literature. A good many of them also were members of the final committee which prepared the National Pharmacopeia.

From New York there were: David Hosack, Samuel L. Mitchell, T. Romeyn Beck, Lyman Spalding, John W. Francis and Valentine Mott. From Massachusetts: John C. Warren, Jacob Bigelow, James Thacher and George C. Shattuck. From New Haven: Eli Ives and Nathan Smith. From Philadelphia: T. T. Hewson and Joseph Parrish. From Maryland: Nathaniel Potter, Elisha De-Butts, Samuel Baker and Ennals Martin.

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## NOTE ON THE ASSAY OF RED CINCHONA BARK.<sup>1</sup>

BY WILLIAM PARTRIDGE.

In the official process of the 1898 British Pharmacopœia for the assay of *Cinchonæ rubræ cortex*, the alkaloids were extracted from the bark by mixing 20 Gm. of the powdered sample with 6 Gm. of calcium hydroxide and 20 Cc. of water. After standing for an hour or two, the resulting moist powder was boiled with benzolated amylic alcohol under a reflux condenser, submitted to two further similar extractions, and then percolated with still more benzolated amylic alcohol.

Benzolated amylic alcohol quickly extracts cinchona alkaloids from a simple aqueous suspension, but from a mixture of bark, calcium hydroxide and water, their extraction is an extremely tiresome process.

In the 1914 edition of the British Pharmacopœia, the same amount (6 Gm.) of calcium hydroxide is mixed with half the quantity (10 Gm.) of powdered bark and slightly more (22 milliliters) water. The result is a paste. Into this 130 milliliters of benzolated amylic alcohol are added, the coherency of the paste is enhanced.

<sup>1</sup> Reprinted from *The Analyst*, March, 1919.

and it appears to be almost undisturbed by the boiling of the solvent. If the boiling be stopped, and the plastic mass be separated into particles with a glass rod, it only requires a gentle rotation of the flask to bring the wet powder to an almost immobile mud again. Subsequent extractions with fresh quantities of the boiling solvent do little to granulate the mud, and after as many as twelve or fourteen percolations the mass is not completely exhausted of alkaloids.

It is better to reduce the amount of water; approximately 12 Cc. of this gives, with 10 Gm. of powdered bark and 6 Gm. of calcium hydroxide, a powder of the right consistency. Using this proportion of water, higher contents of total alkaloids were obtained on three occasions, the increases being respectively 2.02, 1.16 and 1.46 per cent. above the amounts found when the pharmacopœial instructions were followed. All the same, the process remains very tedious.

That the Pharmacopœial Revision Committees have retained Squibb's process (with different modifications) through the 1885, 1898 and 1914 editions, seems to imply a special confidence in it; but as at present described I, at any rate, have not been able to obtain satisfactory results with it.

30, GREAT JAMES STREETS,  
BEDFORD ROW, W.C.I., LONDON.

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## THE DETERMINATION OF ZINC AND COPPER IN GELATIN.<sup>1</sup>

BY GEORGE S. JAMIESON.

One method used for the determination of zinc and copper in gelatin is based upon the complete destruction of the organic matter by digestion with nitric and sulphuric acids.<sup>2</sup> After the digestion is completed, water is added, and the solution is made slightly alkaline with ammonium hydroxide. Then a measured quantity of hydrochloric acid is added. The copper is precipitated as sulphide and filtered. The filter containing the copper sulphide is digested with nitric and sulphuric acids until a colorless solution is obtained. The copper is finally titrated by the well-known iodide and thiosulphate method. When the hydrogen sulphide has been removed

<sup>1</sup> Reprinted from *Jour. of Ind. and Engr. Chem.*, April, 1919. Published by permission of the Secretary of Agriculture.

<sup>2</sup> Methods of analysis, A. O. A. C., 1916, 175.



from the filtrate containing the zinc, ammonium chloride is added along with ammonium hydroxide to make the solution alkaline. Enough hydrochloric acid is added to render the solution acid to methyl orange. After adding a large excess of sodium or ammonium acetate, the zinc is precipitated with hydrogen sulphide and filtered. The zinc sulphide is dissolved in hydrochloric acid and the resulting filtrate is boiled to remove the hydrogen sulphide. A small amount of ferric chloride is added and a basic acetate precipitation is made in the usual manner in order to separate any phosphates present from the zinc. The zinc is precipitated from the filtrate as sulphide and after filtration is ignited to the oxide. It is well known that the digestion of gelatin with nitric and sulphuric acids requires almost constant attention during the entire process which generally takes two hours, and sometimes longer for completion. In addition to the digestion, the long analytical procedure makes the method unsatisfactory.

Several years ago C. R. Smith decomposed gelatin with hydrochloric acid in connection with the determination of arsenic<sup>2</sup> and suggested that this method of decomposing gelatin could be used to advantage for the determination of the other metals in place of the tedious digestion process. Mr. Smith and a number of other chemists have employed the hydrolysis method for the determination of zinc and copper in gelatin. Since the method of separating the zinc from the hydrolyzed solution is somewhat different from that employed in the digestion method, it will be briefly described. A small amount of magnesia mixture and an excess of sodium phosphate solution are added along with enough ammonium hydroxide to make the hydrolyzed gelatin solution alkaline. Then the zinc and copper are precipitated together as sulphides and filtered. The crystalline precipitate of ammonium magnesium phosphate serves to collect the metallic sulphides so that they can be readily filtered. The precipitate is treated with a cold solution of 1:10 hydrochloric acid which has been saturated with hydrogen sulphide in order to dissolve the zinc sulphide and leave the copper sulphide on the filter. The zinc and the copper are determined as described above.

It is believed that the following method will be found much simpler than those now used. The size of the sample taken for analysis varies from 20 to 50 Gm., according to the amount of zinc and copper present. The samples are weighed into 500 Cc. beakers and

treated with 100 Cc. of water and 15 to 30 Cc. of hydrochloric acid, depending upon the amount of gelatin taken for analysis. The covered beakers are heated for an hour or two on the steam bath. During the first part of the heating, the solutions are agitated several times in order to loosen any lumps adhering to the bottom of the beakers. After hydrolysis the solutions are made very slightly alkaline with ammonium hydroxide and allowed to cool to about 40° C. Then hydrogen sulphide is passed into the solutions for 2 min. While passing in the hydrogen sulphide, the solutions should be stirred several times with the delivery tube in order to facilitate the separation of the sulphides in the form most suitable for filtration. When the sulphides have settled for about 10 min., they are filtered on a 9 Cm. filter and washed several times with a very dilute solution of colorless ammonium sulphide. The wash solution is prepared by passing hydrogen sulphide for several minutes into 250 Cc. of water which contains 0.5 Cc. of 1:1 ammonium hydroxide. In the case of high-grade gelatin it is recommended that about 2.5 Mg. of iron should be added to the hydrolyzed gelatin before making the solution alkaline. It is found that ferrous sulphide greatly facilitates the precipitation and the filtration of small quantities of zinc and copper sulphides. The iron is conveniently added in the form of a standard solution which contains 2.49 Gm. of ferrous sulphate in 1,000 Cc. (1 Cc.=0.5 Mg. of iron). If the directions given above are closely followed in making the hydrolyzed gelatin solution very slightly ammoniacal, there is no danger of leaving any weighable amount of copper sulphide dissolved in the ammonium sulphide in the filtrate. The sulphides are dissolved by pouring a small quantity of very hot 1:1 nitric acid around the upper edges of the filters. The filters are washed very thoroughly with water at room temperature. The filtrate is evaporated with 10 Cc. of 1:3 sulphuric acid until all the nitric acid is expelled. When the sulphuric acid is cool, 30 Cc. of water are added, and the solution is filtered to remove the silica. The filtrate, which should have a volume of about 100 Cc. is warmed to about 50° C. and hydrogen sulphide is passed into the solution for at least 5 min. in order to precipitate the copper completely. The copper sulphide is filtered on a Gooch crucible and washed with hot water saturated with hydrogen sulphide. During the filtration and washing of the precipitate a very gentle suction is employed, otherwise there is the danger of having some of the copper sulphide pass through the

crucible. When the washings have thoroughly drained, the Gooch crucible is placed inside of a porcelain crucible and dried over a small flame for a few minutes. Then the flame is gradually increased to its capacity. At this point the outer crucible is removed and the Gooch crucible heated directly in the oxidizing part of the flame for 15 min. After cooling and weighing, the crucible is heated again as hot as possible for 5 min. more in order to be certain that all the copper is converted into the oxide. The filtrate containing the zinc is heated until the hydrogen sulphide is expelled. After adding about 5 Cc. of ammonia in excess of that required to neutralize the sulphuric acid in the solution, 15 Cc. of 50 per cent. formic acid are added and a rapid stream of hydrogen sulphide is passed into the solution for 5 min. to precipitate the zinc sulphide. It is important to stir the solution with the delivery tube while passing in the hydrogen sulphide until the larger part of the zinc is precipitated. The solution containing the zinc sulphide is heated on the steam bath for about half an hour. The zinc sulphide is filtered on a Gooch crucible and washed with a 2 per cent. solution of ammonium thiocyanate. During the filtration and washing of the precipitate, it is best to use either no suction or at most a very slight suction. When all of the precipitate is in the crucible and the wash solution has largely run through, the suction is increased until it is sufficient to drain the crucible properly. The zinc sulphide is dried and ignited to convert it into the oxide in the same manner as the copper sulphide is treated. After weighing, the crucibles containing the oxides of zinc and copper are treated with hydrochloric acid, thoroughly washed with water, and ignited in order to prepare them for subsequent analyses.

Several samples of commercial gelatins of various grades were analyzed by the hydrolysis method described above as well as by the digestion method for the sake of comparison. In the digestion analyses it should be noted that the copper was determined by weighing the oxide in place of the volumetric method given above. Also the zinc was precipitated as sulphide in the presence of ammonium formate and formic acid instead of ammonium acetate and acetic acid.

In conformity to the usual custom, the results of the analyses are stated in terms of milligrams of metal per kilo of gelatin or parts per million.



No.	Hydrolysis Method.		Digestion Method.	
	Cu P.p.m.	Zn P.p.m.	Cu P.p.m.	Zn P.p.m.
1.....	...	1341.0	...	1341.0
1.....	...	1341.0	...	1340.0
1.....	...	1341.0	...	...
2.....	...	126.0	...	122.0
2.....	...	128.0	...	...
3.....	32.0	96.4	32.0	96.4
3.....	26.6	104.0	32.0	96.4
4.....	20.0	64.0	20.0	68.0
4.....	24.0	56.0	20.0	56.0
5.....	24.0	77.9	24.0	80.3
5.....	22.4	80.3	24.0	80.3
5.....	20.0	80.3	...	76.0

The copper was separated but was not determined in samples 1 and 2 because at first it was intended only to investigate the determination of zinc.

In order to test the method further, measured quantities of standard solutions of zinc and copper were added to weighed amounts of sample 5. The hydrolysis and analyses were made as described above with the following results:

Sample Taken, Grams.	Cu Added, Mg.	Zu Added, Mg.	Cu Found, Mg.	Zu Found, Mg.
20	2.5	2.8	2.5	2.7
20	3.0	3.1	3.1	3.2
20	2.5	4.7	2.4	4.7
20	2.0	3.1	1.9	3.2

It should be observed that the amount of zinc and copper in 20 Gm. of sample 5 gelatin as determined by averaging the results obtained by previous analysis, has been deducted from the results given above. The results obtained with these analyses show that the method is accurate.

In order to obtain satisfactory results, it is most important that the directions be followed in every detail. Furthermore, great care must be taken to eliminate by filtration any non-volatile matter which may separate during the course of the analyses, before proceeding to make the final precipitation of the zinc or copper sulphides. Also, the Gooch crucibles used must be prepared so that they will not lose weight during the filtration and ignition of the sulphides.

BUREAU OF CHEMISTRY,  
DEPARTMENT OF AGRICULTURE,  
WASHINGTON, D. C.

SCAMMONY AND ITS SUBSTITUTES.<sup>1</sup>

BY W. L. SCOVILLE.

There was recently received from a New York broker a sample of a Mexican plant known as *Resina drastica*, with the statement that several hundred pounds of it were available, and asking for an offer for the lot. The drug so closely resembled that known as Mexican scammony, *Ipomœa orizabensis*, as to be mistaken for that drug on quick inspection by our botanist.

On extracting the ground drug with alcohol it was immediately evident that something different from Mexican scammony was at hand, for the percolate was a deep yellow in color, and when it was concentrated and poured into acidulated water a bright lemon-yellow resin was obtained. This resin amounted to 19.2 per cent. of the drug taken. The alcoholic solution showed 23.5 per cent. of total extractive from the drug.

A comparison of the chemical characters of the resin with true resin of scammony, *Convolvulus scammonia*, and with the resin of Mexican scammony disclosed the following:

	Resin of Scammony.	Resin of Mexican Scammony.	Resin of <i>Resina drastica</i>
Yield, per cent.....	About 8	9 to 20	19.2
Color .....	Yellowish- brown	Straw	Lemon-yellow
Ash .....	Practically none	Practically none	Practically none
Solubility in			
Petroleum ether .....	3.5 per cent.	2.5 per cent.	1.0 per cent.
Ether .....	Soluble	Soluble	72.6 per cent.
Acetic ether .....	Soluble	Soluble	Soluble
Chloroform .....	Cloudy soln.	Cloudy soln.	94 per cent.
10 per cent. ammonia .....	Cloudy soln.	Cloudy soln.	Cloudy soln.
10 per cent. potassium hydroxide solution .....	Cloudy soln.	Cloudy soln.	Cloudy soln.
Acid number .....	20	23.5	28.0
Saponification number.....	198	140	136
Optical rotation .....	— 17.3	— 24.8	— 32.4
Color with FeCl <sub>3</sub> .....	Dark green	Faint green	Dark green

The optical rotation of true scammony resin obtained from the root is reported by P. Guigues to vary from  $-18^{\circ} 31'$  to  $-23^{\circ} 30'$  and the upper limit of natural scammony resin as  $-25^{\circ}$ . Resins having a rotation of  $-23^{\circ}$  to  $-25^{\circ}$  are considered to be derived from *Ipomœa orizabensis*.

The resin of *Resina drastica* is less soluble in ether and in chloro-

<sup>1</sup> Reprinted from *Jour. Ind. and Engr. Chem.*, April, 1919.

form than is true scammony resin or the Mexican scammony resin. It is more slowly soluble in alkalis than is true scammony resin, as also is that of the Mexican scammony. All three gave markedly cloudy solutions in ammonia and in potassium hydroxide solution, but the insoluble portions were so fine that the solution passed through an analytical filter without clearing and without collecting an appreciable residue on the filter. Acidulating the alkaline solutions did not precipitate the resin in any case.

The alcoholic solution of *Resina drastica* reduced Fehling's both before and after heating with weak sulphuric acid. It is thus uncertain whether the resin has a glucosidal character or not.

The supply was limited and a separation plan could not be carried out.

In general character, this resembles both true and Mexican scammony resins. It is slightly more acid and is more strongly levorotatory. Its color alone would distinguish it, and treatment with decolorizing charcoal does not take out the color appreciably. When freshly precipitated it has an agreeable tea-like odor which disappears on drying. Probably a small amount of volatile oil is present in the drug. The powdered resin resembles scammony resin in odor.

The special distinguishing features of the three resins are: (1) The brownish color of true scammony resin, and the very deep green color which it gives with iron salts, (2) the light color of Mexican scammony resin, producing a colorless alcoholic solution, and giving almost no color with iron salts and (3) the deep lemon-yellow color of the *Resina drastica*.

The iron test distinguishes quite sharply between true and Mexican scammony when a ferrous salt is used. If 0.5 Gm. of the resin be dissolved in 10 mls of alcohol and 0.5 ml of a 10 per cent. aqueous solution of ferrous sulphate added, the Mexican scammony resin shows only a very faint green while the others become dark green and on standing deposit a dark mass, leaving an olive-green supernatant liquid.

Subsequent efforts to obtain another sample of the *Resina drastica* for botanical study have failed, though samples of drugs having a different character were sent. It seems probable that several botanical species, closely allied, are seeking a market as scammony or scammony substitutes.



THE USE OF ORTHO-TOLIDINE AS A COLORIMETRIC TEST FOR GOLD.<sup>1</sup>

BY W. B. POLLARD.

Ortho-tolidine dissolved in dilute acetic acid was suggested by E. B. Phelps<sup>2</sup> as a delicate color test for free chlorine in water. This test was modified by J. W. Ellms and S. J. Hauser,<sup>3</sup> who showed that a hydrochloric acid solution of ortho-tolidine was better adapted for the purpose. Their reagent was prepared by dissolving one Gm. of ortho-tolidine in a liter of 10 per cent. hydrochloric acid.

The reagent in its modified form has now been found to be a delicate test for aurichloric acid. A solution of 1 part of gold in a million parts of water gave a bright yellow color on addition to 1 Cc. of the reagent. With a solution containing 1 part of gold and 20 million parts of water the yellow color can just be detected in a depth of 10 Cm. of liquid.

Ellms and Hauser found that in the case of dilute solutions containing free chlorine the color took about three minutes to fully develop, and was then permanent for about half an hour, after which it slowly faded. This was also found to be the case with aurichloric acid.

In making the test large amounts of strong mineral acid should not be present as the reaction becomes less delicate.

The following metals when present as chlorides in a dilute hydrochloric acid solution, were found to give no reaction with ortho-tolidine: Al, Sb (ic), Ba, Bi, Cd, Ca, Cr, Co, Cu, Ir, Pb, Mg, Hg, Mn (ous), Ni, Pt, K, Rh, Na, Sr, Sn (ic), U and Zn.

In a second paper Ellms and Hauser point out that iron in the ferric condition also reacts with ortho-tolidine. The author found that in the case of ruthenium a yellow color was also formed. Osmic acid gives a yellow color, but this changes to a green on standing. Vanadates acidified with dilute hydrochloric acid give a reaction. Molybdates acidified with hydrochloric acid do not react.

Sodium tungstate acidified with dilute hydrochloric acid gives a precipitate on addition of ortho-tolidine, but no yellow color develops.

<sup>1</sup> Reprinted from *The Analyst*, March, 1919.

<sup>2</sup> Bulletin No. 1, Ohio State Board of Health, January, 1913.

<sup>3</sup> *Analyst*, 1914, 39, 454.

In preparing standard chlorine solutions, Ellms and Hauser found that it was necessary to employ specially purified distilled water.

This was not found to be so necessary in the case of gold solutions. The more dilute gold solutions should, however, only be prepared when required, and should contain a small amount of free hydrochloric acid.

In testing solutions which have been obtained by the use of aqua regia, special care should be taken to guard against the possible presence of free chlorine, or of nitrous acid. The latter not only reduces gold solutions, but gives a yellow color with ortho-tolidine. Any reagents used should always be tested for reducing impurities; thus, on one occasion a sample of "pure" ammonium chloride completely reduced a weak gold solution.

In presence of much copper a green color is obtained instead of a pure yellow; colorimetric comparison can, however, still be made if the standard gold solution is tinted with copper to a similar extent.

GOVERNMENT ANALYTICAL LABORATORY,  
CAIRO.

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## THE MANUFACTURE OF PHARMACEUTICAL PRODUCTS IN FRANCE.<sup>1</sup>

That French manufacturers of pharmaceutical products are confronted with the same problems and difficulties as their British *confrères* is disclosed in a well-informed article by Monsieur A. Detoef in the February issue of *Chimie et Industrie*.

In discussing the future of this industry, M. Detoef states that the pre-war idea that the French were tributaries to Germany for the greater part of their pharmaceutical products did not quite correspond to reality. He points out that two distinct classes must be recognized among medicinal products, based on the existence or non-existence of patents and trade-marks which enable the manufacturer to defend his products against competition. The French patent law of 1844 at present in force excludes medicinal products, but in practice this restriction is often overcome by taking out a

<sup>1</sup> Reprinted from *The Journal of the Society of Chemical Industry*, April 20, 1919.

process patent to cover the preparation of a substance which is the eventual "raw" material of a medicinal derivative; and with regard to the trade-mark, it is well recognized that a simple denomination authorized for pharmaceutical products, which is renewable indefinitely, confers on its possessor an equally indefinite proprietary right.

By reason of these prerogatives there are two clearly defined classes of medicinal products: (1) Those not protected by any mark and of which the manufacture has either never been covered by patents, or is now protected by patents; (2) those put on the market under a mark and of which the manufacture is also protected by patents.

1. Practically all these products are listed in the official Pharmacopœia, and a large proportion of them was made in France before the war. Among the products belonging to mineral chemistry we find such important substances as potassium permanganate, corrosive sublimate and the bichromates of potassium and sodium. The manufacture of saccharin requires large quantities of permanganate, and this must be produced in sufficient quantity to meet all future requirements. Small quantities of corrosive sublimate have been made in France, although the manufacture depends, apart from the supply of mercury, on the available quantities of chlorine. No doubt the electrolytic works, now free from war restrictions, will soon be equal to meeting the entire home consumption. Bichromates constitute a very necessary raw material for the manufacture of many products, and a trial factory has been established in France during the war. This requires patent development in order to free France from foreign influence.

The following organic products—and these constitute the majority—were not made in France before the war, or were made in works now destroyed:—Chloral, valerianic acid and valerianates, monochloroacetic acid, oxalic acid and oxalates, phosgene, urea, morphine, codeine and derivatives, phenol, guaiacol and salts, benzoic acid and benzoates, saccharin, phthalic acid and phenolphthalein. With the exception of morphine and its derivatives and chloral (which were not manufactured for special reasons), all the other products named have been manufactured in France during the war. It cannot be said, however, that these have yet been produced under the most economic conditions, and it is therefore uncertain if the manufacture can be maintained. The production of



nearly all these organic products depends upon a cheap supply of primary materials, such as mineral acids, caustic alkalis and chlorine. These materials are likewise used in the manufacture of aniline colors and synthetic perfumes, and it is in this whole field that development is needed, for the production of pharmaceutical products is only auxiliary to the manufacture of dyes.

It was principally from the German chemical dye works that pharmaceutical products were issued before the war. One great service which the war has rendered to France (and incidentally to Great Britain) is that it has made both nations producers of these primary materials at first hand. The factories that have produced for war must now produce for peace. Works that can produce electrolytic chlorine cheaply will be best able to make chloral, monochloroacetic acid, benzoic acid and phosgene. The present makers of benzene and phenol can turn out guaiacol and its derivatives most successfully. From cyanamide, urea can be obtained; from toluene, saccharin; from naphthalene and oleum, phthalic acid; from amyl alcohol, valerianic acid; and so on.

But although it is necessary to encourage by all possible means the development of chemistry in France, it is no less indispensable to warn manufacturers that pharmaceutical products cannot be produced with a small plant and scant material. They require a perfected plant, the processes must be scrupulously attended to, and above all there must be facilities for disposing of the by-products to good account. "One does not manufacture a pharmaceutical product," says M. Detoef, "one manufactures all the products appertaining to the same series and dependent on the same crude material."

2. It was by means of trade-marked or patented medicinal preparations that the Germans formerly invaded the French market. With the German manufacturer every new organic or mineral derivative was a potential material for a medicament. Intensive research in the factory laboratories and systematic experiment in their laboratories of therapeutic physiology, enabled them to recognize to a certainty such products as were endowed with special therapeutic activity. The process of manufacture was then patented in Germany, and if possible in France, no mention being made of therapeutic properties. Then the product was put on the market under cover of a *marque déposée* and introduced to medical men.

The pre-war attitude of the French manufacturer was that if the German product had a small sale he left it alone. If, on the contrary, the sale developed the French manufacturer produced a preparation of the same chemical composition and put it on sale either under its chemical name or under another name chosen by himself. In every case the use of the German trade-mark was denied him as constituting an international industrial property. This explains why before the war only such products which could by their popularity justify the expense and risk of their production were manufactured in France.

Among the more important of the organic or mineral products sold under a German mark were: Adalin, anæsthesin, antipyrine, aristol, aspirin, atophan, bismon, bornyval, bromipin, bromural, citrophen, collargol, creosotal, dermatol, dionin, diuretin, euquinine, helmitol, heroin, lactophenin, luminal, lycetol, lysol, salvarsan and neosalvarsan, novocain, orthoform, phenacetin, protargol, pyramidon, salophen, somatose, sulphonal, trional, urotropin, veronal, xeroform. Of these all except anæsthesin, atophan, bismon, bornyval, citrophen, phenacetin, salophen, somatose, sulphonal and trional, are now made in France.

In suppressing German competition, the war has made it comparatively easy to launch on the market, under a new trade-mark name, certain of these products which are still in demand among medical men. On the other hand, some French manufacturers before the war were able to secure by judicial action that certain marks which had become the usual name of the product (for instance, antipyrine, pyramidon, etc.) should be put into general use.

Two ways are open to French manufacturers: either they can reproduce chemically the German products and face the competition, or they may build up new compounds of proved therapeutic properties and place them before the medical profession. The difficulties of the task must not be overlooked. Well-equipped laboratories are necessary, manned by chemists trained to research, particularly in organic chemistry, and, above all, the possibilities of physiological experiment must be attended to. On the other hand, the industry in pharmaceutical products sold under a trade-mark requires usually but a small, though perfect, plant, and there is less risk of such trade being submerged by the dye and synthetic perfume industries.

M. Detoef's illuminating review of the situation shows quite

clearly that the question of the manufacture of pharmaceutical products is not so simple or so attractive as is often believed. New-comers, he says, will find themselves very quickly in the presence of difficult situations, and bitter competition awaits them, both at home and abroad. It is imperative, he concludes, that the laws now under consideration regarding patents and trade-marks should ensure to these manufacturers sufficient guarantees for their enterprise without harm to the general interest. It is also necessary that they should be kept well informed of everything that is being done at home and abroad, and that official science should support them openly and without expectation of immediate reward. Finally, as the pharmaceutical industry, like other industries, has given the state all possible assistance during the war, it is the duty of the state to protect it now.

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## STANDARDIZING DISINFECTANTS.<sup>1</sup>

Dr. Samuel Rideal communicates to the *British Medical Journal* the following details of the standard bacteriological test (Rideal-Walker Method) adopted by the members of the British Disinfectant Manufacturers' Association: Well shake the bottle or other vessel containing the disinfectant before proceeding to make the dilution. Make a 1 per cent. stock emulsion (5 Cc. of disinfectant added to 495 Cc. of boiled distilled water of 15° C. to 18° C.). From this stock emulsion prepare required dilutions in boiled distilled water, taking care that pipettes used for preparing stock emulsion as well as dilutions are, after emptying, always well washed out with and into the diluent, and that all dilutions, including stock emulsion, are well shaken before use. To 5 Cc. of a particular dilution add 0.2 Cc. (5 drops) of a broth culture of *B. typhosus* grown for twenty-four hours at 37° C. Shake immediately after medication. Keep medicated tubes at temperature of 10° C. to 18° C. and take subcultures into 5 Cc. broth every two and a half minutes up to ten minutes. Incubate for a least forty-eight hours at 37° C. Rideal and Walker, (*J. S. I.*, October, 1903, p. 424), use as stock organism *B. typhosus* from a single colony on an agar plate culture that has been grown at 21–22° C. from two to seven days and removed by weekly transference for several uninterrupted genera-

<sup>1</sup> Reprinted from *The Chemist and Druggist*, April, 1919.



tions from the original source (the human body). Owing to the extremely important influence which the broth has on the characteristics of the *B. typhosus* employed as the test organism in the Rideal-Walker test, *particularly as regards the peptone*, attention is drawn to the fact that this is prepared according to the following modification of the formula of Dr. S. Rideal (Fourteenth International Congress for Hygiene and Demography, Berlin, 1907):

Lemco, 20 Grams. Peptone (Allen & Hanbury's "Eupepton") 20 Grams. Sodium chloride, 10 Grams. Water to 1 liter. Boil the mixture for thirty minutes, neutralize with normal caustic soda (phenolphthalein indicator); add 15 cubic Centimeters of normal hydrochloric acid; make up to 1 liter with distilled water, filter, and finally sterilize.

The culture employed must conform with the requirements laid down by the authors of the test (*v. Lancet*, September 25, 1915, p. 717)—viz., "Life in two and a half minutes and five minutes and no life thereafter," with "phenol dilutions not higher than 1:110 or lower than 1:90."

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## ANNOUNCEMENTS.

### THE UNITED STATES PHARMACOPŒIAL CONVENTION OF 1920.

Article VIII, Chapter I of the By-Laws of the United States Pharmacopœial Convention provides that the president:

"shall issue, on or about the first of May of the year immediately preceding that of the decennial meeting, a notice inviting the several bodies, entitled under the Constitution to representation therein, to send delegates to the next meeting. He shall repeat the notification, eight months later, and shall request the medical and pharmaceutical journals of the United States to publish the call for said meeting."

Article II of the Constitution provides:

"The members of the United States Pharmacopœial Convention, in addition to the Incorporators and their associates, shall be delegates elected by the following organizations in the manner they shall respectively provide: Incorporated medical colleges, and medical

schools connected with incorporated colleges and universities; incorporated colleges of pharmacy, and pharmaceutical schools connected with incorporated universities; incorporated state medical associations; incorporated state pharmaceutical associations; the American Medical Association, and the American Chemical Society; provided that no such organization shall be entitled to representation unless it shall have been incorporated within and shall have been in continuous operation in the United States for at least five years before the time fixed for the decennial meeting of this corporation."

Section II of the Constitution provides:

"Delegates appointed by the Surgeon-General of the United States Army, the Surgeon-General of the United States Navy, and the Surgeon-General of the United States Marine-Hospital Service, the Secretary of Agriculture, the Secretary of Commerce and Labor, the Association of Official Agricultural Chemists, the Associations of State and National Food and Dairy Departments, the National Wholesale Druggists Association, and the National Dental Association, and by the organizations not hereinbefore named which were admitted to representation in the Convention of 1900, shall also be members of the corporation. Each body and each branch of the United States Government above mentioned shall be entitled to send three delegates to the meetings of this corporation. But no such delegates as are provided for in this article shall be members until their credentials shall have been examined and acted upon as provided for by the By-Laws."

In the discharge of the above required duties, I hereby ask all competent and designated bodies and authorities to name and issue credentials to the fixed number of delegates to the tenth decennial Convention to meet in Washington, D. C., on the second Tuesday of May, 1920, at 10 o'clock a.m. at a hall to be designated hereafter. The appointed delegates are requested to promptly forward their credentials to Noble P. Barnes, M.D., The Arlington Hotel, Washington, D. C., assistant secretary of the Convention, who will file them for consideration of the Committee on Credentials which will be appointed by the president not later than March first, 1920, according to the requirements Chapter VII, Article I of the By-Laws.

Done at Washington, D. C., May 5, 1919.

HARVEY W. WILEY,

*President of the United States Pharmacopœial Convention.*

## A GRANT FOR RESEARCH.

The American Pharmaceutical Association has available a sum amounting to about \$240.00 which will be expended during 1919-1920 for the encouragement of research. This amount either in full or in fractions will be awarded in such manner as will in the judgment of the A. Ph. A. Research Committee produce the greatest good to American pharmaceutical research.

Investigators desiring financial aid in their work will communicate before August first with H. V. Army, Chairman A. Ph. A. Research Committee, 115 W. 68th St., New York, giving their past record and outlining the particular line of work for which the grant is desired.

The committee will give each application its careful attention and will make recommendations to the American Pharmaceutical Association at its meeting in New York, August 25-29, 1919, when the award or awards will be made.

PHILADELPHIA DRUG EXCHANGE APPEALS FOR  
REDUCTION IN THE NUMBER OF NARCOTIC  
DRUG FORMULÆ.

At a meeting of the board of directors of the Philadelphia Drug Exchange held on May 14, 1919, a motion was passed directing the secretary to communicate with the American Drug Manufacturers Association and other drug manufacturing bodies, calling attention to the apparently needless multiplication in the price lists of manufacturing pharmacists of narcotic drug formulas of many unnecessary strengths, urging that the number be minimized to the fewest possible units, so that the burden of making out the federal and state narcotic reports be reduced to the lowest possible limit.

Thus, for example, in the price list of a prominent manufacturer there are of hypodermic tablets of morphine, plain and combined, 37 strengths; of heroin, 5 strengths; of diacetylmorphine, 4 strengths; of codeine, 6 strengths; of cocaine, 8 strengths. There are 72 items in the list of hypodermic tablets subject to the Harrison law. In the same list, under tablet triturates there are 99 items; under compressed tablets, 43 items; under chocolate coated tablets, 54 items; under dispensary tablets, 8 items; under pills, 49 items; a total in



all of 385 items, and this does not include elixirs and other forms of galenicals, nor the items of the price lists of other manufacturers not mentioned in the list referred to. Hence, it is apparent that druggists are compelled to stock and report upon hundreds of narcotic preparations, many of which could be eliminated from the lists and the burden of the wholesaler and retailer lightened.

We respectfully ask, therefore, that the members of your organization give consideration to the desirability of standardizing the lists of the preparations referred to by minimizing the number of items of narcotic products to the end that the details of keeping narcotic records may be simplified and time and work saved.

Of course, we realize that there are trade demands which necessitate the listing of many narcotic products, but we believe that there is a marked tendency in the medical profession towards the much-lessened use of narcotic drugs in the treatment of disease, and that the medical profession would not seriously object to the excision of many narcotic formulas from the lists, and they would not be denied the use of such narcotic drugs as they could readily have them compounded extemporaneously.

## GRAND CENTRAL PALACE, NEW YORK, TO BECOME A WORLD TRADE MART.

### GOVERNMENT TO TURN BUILDING BACK TO MERCHANTS AND MANUFACTURERS EXCHANGE.

One of the biggest enterprises to be embarked upon, having in mind the extension of American commerce in foreign countries, as well as the importation of foreign goods to America, has just been inaugurated in New York City. It is the new proposition of the Merchants and Manufacturers Exchange of New York to make Grand Central Palace a great clearing house for world commerce.

On September 30, the United States Government will turn Grand Central Palace back to the Merchants and Manufacturers Exchange. For months this great twelve-story building—the largest exposition building in the world—which occupies an entire city block, has been used as an army base hospital. Its evacuation, now taking place, will permit reconstruction of the entire interior so as to make it ideal as a permanent show place for all sorts of manufactured

products. The industries will be grouped and permanent exhibits will be made on eight spacious floors, each floor having approximately 60,000 square feet of space. The remainder of the building (the four lower floors) will be utilized for the annual expositions which have made the building famous, such as the Automobile Show, Motor Boat Show, Flower Show, Electrical Exposition, Chemical Exposition, Hotel Men's Exposition, etc.

Permanent exhibits of products of the more important industries will be opened beginning October 15. The Merchants and Manufacturers Exchange has established foreign connections for export business in every important city of the world, and manufacturers, jobbers, retail dealers, and the thousands of foreign buyers undoubtedly soon will regard Grand Central Palace as the world's great trade center and will make it their headquarters when visiting New York. Looking forward to this the management will establish club rooms, conference rooms, office facilities, etc., to increase the foreign buyers' comfort while in the metropolis.

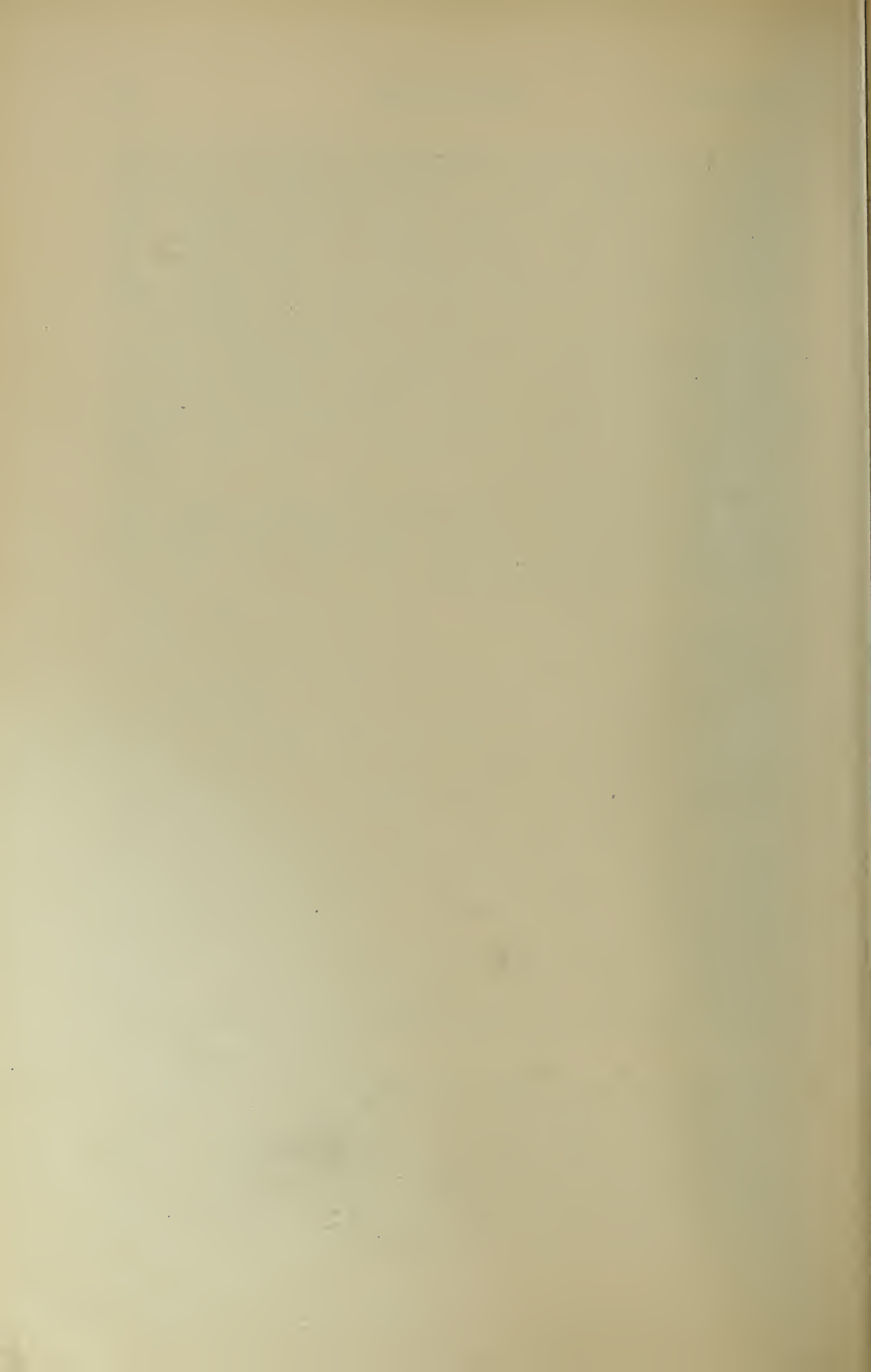
Never before has there been such a permanent exchange conducted along international lines which will give the American manufacturer an opportunity to come into direct contact with the domestic and foreign buyer. Some of the industries represented will occupy an entire floor, such as The International Farm Tractor and Implement Exchange, the International Hardware and Homefurnishings Exchange, which will be among the first to be opened, on the sixth and seventh floors respectively. Other enterprises under way for other floors are a permanent Mining Machinery Exposition, a Railway Equipment Exposition, Textile Display, Printing Trades Exhibit, etc. The Farm Tractor Exchange and the Hardware Exchange will open on October 15, 1919. The plans of the Merchants and Manufacturers Exchange are decidedly elaborate, and in a number of ways they will afford a service to the manufacturer, jobber and dealer which has never been possible under the usual systems of merchandizing.

Through its wide representation in other countries the exchange will make its proposition known to every foreign buyer before he sails for America and acquaint him with the value of the service of the new enterprise, while in the United States and Canada the fact that the building is so well known leaves no doubt that it will be the mecca of thousands of domestic dealers and jobbers.

In spite of the fact that the building is an enormous one, space necessarily is limited and manufacturers interested in putting their products before the eyes of buyers in this highly convenient manner will have to step lively to secure space on the various floors. Only goods of proven quality and concerns of A-1 repute will be permitted to exhibit. Grand Central Palace, which is a beautiful building in itself and prior to the entry of the United States into the war, housed the largest expositions held in New York, is centrally located and most convenient to all railroads, steamship piers, hotels, theaters, and the shopping district. The march of the world's industrial progress during the reconstruction period will be largely via Grand Central Palace.

Detailed information may be obtained by addressing the Merchants and Manufacturers Exchange, 405 Lexington Avenue, New York, Room 421, prior to October 1; after that date headquarters will be in the Grand Central Palace.





# THE AMERICAN JOURNAL OF PHARMACY

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*JULY, 1919*

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## EDITORIAL.

### THE PHARMACEUTICAL SIGN-BOARDS ALL POINT TOWARD NEW YORK.

The sixty-seventh Annual Convention of the American Pharmaceutical Association to be held in New York City during the week commencing August 25, bids fair to be a most memorable occasion. The headquarters will be at the new and commodious Hotel Pennsylvania, said to be the largest and most modern hotel structure in the world.

The Local Committee advises that the management of the hotel has promised to supply the best of facilities for the meetings of the Association and its Council and Committees and the various allied organizations that are scheduled to meet during the same week and the best service that New York can supply. Notwithstanding the many hostelries of the metropolis, the demand for hotel accommodations in New York has at times, during the recent years, exceeded the rooms available. Hence, despite the enormous size of the Hotel Pennsylvania, the local committee advises that reservations for the week of the convention be made early.

In celebration of the "Victory Year" special consideration is to be given to the entertainment features and the ladies are especially invited to attend and these functions are guaranteed to make their visit to New York enjoyable and a pleasant memory for all time to come.

The various Sections and Committees are earnestly working to present interesting and progressive programmes. The chairman of the Scientific Section writes that it is the intent to devote the entire time of one of its sessions to the consideration of the scientific

phases of pharmacopœial revision and that papers on the leading topics of the pharmacopœia will form the basis for this discussion. This should prove both timely and profitable as we are rapidly approaching the date set for the meeting of the Pharmacopœial Convention.

The pre-convention announcement of the Section on Commercial Interest shows a well-selected list of topics including addresses by several teachers of scientific commercial education in prominent universities.

Dr. Henry M. Whelpley will deliver before the Historical Section one of his brilliant lectures. He is a past master in all matters relating to the lore and customs of the American Indian. In fact he is accredited with being one of the "Two Big Indian Chiefs of Missouri."

Equally interesting and instructive programmes are offered by the Sections on Education and Legislation and of Practical Pharmacy and Dispensing and it goes without saying that the Women's Section will not be behind the other sections.

Besides all of these announced topics there are many subjects and events affecting pharmacy in this period of great reformation and world recasting that are sure to be discussed as well as many other matters that may be considered as purely intra-association.

The pharmacist who misses this meeting will ever regret it. The Local Committee have laid their plans for a largely attended, enthusiastic "Victory Meeting" and the pre-convention arrangements all indicate a fine and continuous feast of knowledge and enjoyment.

G. M. B.

### JOURNALISTIC COURTESY.

Strange as it may appear to some, the editor of a magazine, journal, newspaper, or a publication of any standing whatever, appreciates that he has responsibilities, both moral and material, that he must discharge. Hence, there are certain well-known principles of journalism that belong properly to the editors' code of ethics. Not the least of these is to keep his publication free from the charge of plagiarism.

There are two underlying reasons that make such a course of procedure essential and both of these are based upon the principle



of common honesty. Journalistic courtesy alone should determine that due credit be given alike to the author and to the source of original publication and any other course is simply the appropriation of another's rights and property and a violation of this law of the decalogue. Moreover, the palming off of a prior publication as an original contribution of the author or even the abstracting of an article without giving credit to the original publication, is a deliberate act of deception practiced against the subscribers of the journal and is even less pardonable than the ordinary deceptions of trade.

The AMERICAN JOURNAL OF PHARMACY scrupulously adheres to the principle of giving with each article the source of the original publication and, if an abstract, tracing wherever possible the course of the preparation of such abstract. This is simply an upright recognition of our obligation to be honest with authors and readers alike and an observance of the just rule to give honor and credit to those to whom such is due. It is not the intent of the publishers of this JOURNAL to claim absolute ownership of the papers and contributions published originally therein. Neither is it our purpose to copyright or otherwise limit republication. To the contrary we welcome the widest distribution of every item of information of value to pharmacists or others and after publication the articles are subject to such use. We do, however, insist that in all such republications of papers and articles originally published in the AMERICAN JOURNAL OF PHARMACY there should be appended a statement crediting the original publication.

We recognize that most of the contemporary pharmaceutical journals are conscientiously observing this principle of journalistic courtesy. A study of the current literature will, however, show that there are a few editors who are negligent and at times exceedingly careless in their observance of this editorial propriety. There is now before the writer a current pharmaceutical journal whose pages are almost entirely filled with copied articles for which, with one exception, no credit is given to the original publication and of these three are copied from the pages of the AMERICAN JOURNAL OF PHARMACY. A most charitable view will not permit one to attribute such an example of plagiarism to "subconscious absorption."

G. M. B.

## HOW PHARMACISTS MAY OBTAIN DISTILLED SPIRITS AND WINES FOR MEDICINAL AND PHARMA- CEUTICAL PURPOSES.

The prohibition wave that has overflowed our country with its associated extreme, yet imperfect, legislation has created new problems and difficulties for pharmacy. With the sale of beverage spirits of any kind whatsoever, either distilled, vinous or malted we are not at all concerned. In our opinion ethical pharmacy has nothing whatever to do with the sale or handling of beverage liquors and any pharmacist who will sell his professional birthright by engaging in such traffic should have his license to practice pharmacy cancelled and he should forever be debarred from the profession that he has disgraced.

The zealot, blinded by ignorance or bigotry, may fail to appreciate the indisplaceable position that alcohol holds as an essential ingredient for the preparation or preservation of many medicines. Many of the propositions submitted in Congress and in the State Legislatures are exhibitions of fanaticism and woeful ignorance of the needs of medicine and pharmacy. It is fortunate that, up to the present time, the rational legislators have been in the majority and the several federal acts as well as the prohibition Amendment to the U. S. Constitution recognize that there are legitimate uses in medicine for distilled spirits and wines and exempt from the severe provisions of these laws such for "*medicinal*, and other non-beverage purposes."

Our investigations convince us that the preponderance of opinion among practicing physicians is that there is a legitimate and necessary use for certain distilled spirits and wines as medicinal agents. To the ethical physician and pharmacist distilled or vinous spirits have no other significance than that of articles of *materia medica*. When indicated in the judgment of the physician he will prescribe these and the prescriptions for such will be compounded just the same as in other cases where he may prescribe epsom salt, potassium bromide or nux-vomica.

As representing pharmaceutical and medical interests we are concerned when the *materia medica* is restricted by either legislation or departmental regulation. To jeopardize the lives of our sick by restricting the remedial agents at the command of the physician would be a national crime and not less heinous because dictated by radicalism and fanaticism.

Wines have been used as solvents or vehicles for medicines from time immemorial and for some years past the Federal Departments, for economic reasons, have encouraged the use of native wines in the preparation of medicines and other manufactured products. As a result of established custom and stimulated consumption there are in use many formulas in which wine is an essential ingredient and nearly a score of such formulas are officially recognized in the National Formulary.

So it became a question of importance to pharmacists as to how they are to secure supplies of non-beverage distilled spirits and wines for dispensing on legitimate prescriptions and likewise that needed for manufacturing the formulas of the N. F. as well as those of foreign pharmacopœias and formularies in which wine is directed. The Internal Revenue Department has a difficult task to perform in the framing of regulations that will permit of the use of alcohol, potable distilled spirits, and wines for purely medicinal uses and exclusively non-beverage purposes and at the same time protect against fraud and violation of the acts and in this they should have the most cordial support and coöperation of pharmacists.

Our sense of duty in this matter, we believe, justified the taking up of various phases of this question with the officials of the Department by interview and correspondence and the offering of suggestions by which pharmacists who have given bond and have permit to withdraw non-beverage alcohol for use and sale may have such bond and permit extended to cover likewise the withdrawal of non-beverage potable distilled spirits and wines for purely medicinal and pharmaceutical purposes.

The following copies of portions of the correspondence relating to the pharmaceutical uses of wines are published for the advice of pharmacists.

June 6, 1919.

HON. H. M. GAYLORD,  
Deputy Commissioner of Internal Revenue,  
Treasury Department,  
Washington, D. C.

*My dear Sir:*

Pursuant to your request in our recent interview, I have decided to address two distinct letters to you, this one relating to the prob-



lems confronting pharmacists and the Committee on Revision of the National Formulary concerning the use of wines for manufacturing the formulas of the National Formulary and other formularies and pharmacopœias in order that your ruling on this point may be placed before the Committee on Revision of the National Formulary.

In my former letter of April 17, 1919, addressed to the Hon. Daniel S. Roper, Commissioner of Internal Revenue, I propounded the following distinct query:

“Will pharmacists be permitted under their bond covering the use of non-beverage alcohol to likewise withdraw non-beverage wines for the purpose of manufacturing these formulas, and the formulas for medicinal wines official in some of the foreign pharmacopœias, which in this country are more or less prescribed on prescriptions?”

As no ruling has yet been promulgated on this point, I am repeating the query in accordance with our understanding so that it may receive your personal consideration and decision.

I trust that this will be rendered at an early date so the information may be imparted to the members of the Committee on Revision of the National Formulary and likewise to the pharmacists who are necessarily interested.

I am,

Very truly yours,

GEORGE M. BERINGER,  
*Editor.*

TREASURY DEPARTMENT.

WASHINGTON, D. C.,  
June 16, 1919.

GEORGE M. BERINGER, *Editor*,  
American Journal of Pharmacy,  
145 N. 10th Street,  
Phila., Pa.

*Sir:*

Receipt is acknowledged of your letter dated June 6, 1919; in which you ask whether pharmacists will be permitted under their bond covering the use of non-beverage alcohol, to likewise withdraw non-beverage wines for the purpose of manufacturing formulas of the National Formulary and other formularies and pharmacopœias; and also whether non-beverage wines may be used in formulas for

medicinal wines official in some of the foreign pharmacopœias, which in this country are more or less prescribed on prescriptions.

In reply your attention is called to T. D. 2788, copy of which is enclosed, from which you will note that, in order to be entitled to obtain non-beverage wines for the purposes mentioned in your letter, it is necessary to qualify by obtaining permit and giving bond. The bond given covering the use or sale of non-beverage spirits is not sufficient to cover, in addition, the use or sale of non-beverage wines, and therefore, if it is desired to use or sell both spirits and wines it will be necessary to give a bond covering both these articles in the form prescribed in the above Treasury Decision. Also a permit must be procured covering the use of non-beverage wines in specific preparations, for, as in the case of non-beverage spirits, non-beverage wines may be used only as expressly stated in the permit.

Non-beverage wines may be in the production of medicinal preparations, including those official in some of the foreign pharmacopœias, not contained in the U. S. P. or N. F., provided the sworn data and samples called for in T. D. 2788 are submitted, and permit is obtained and bond filed covering the manufacture of such preparations.

An additional letter dated June 6, 1919, has also been received by this Bureau from you, in reference to the use of potable distilled spirits and wines as such for medicinal purposes. This letter will be considered by this Bureau and you will be advised at a later date of the conclusion reached.

Respectfully,

(Signed) H. M. GAYLORD,  
*Deputy Commissioner.*

As a necessity, most pharmacists have already given bond and obtained the permit to obtain alcohol for sale or use as non-beverage spirits but as a rule the form used did not cover the use or sale of non-beverage wine. From the above decision, it is apparent that to secure wines for the *purpose of manufacturing* non-beverage articles, such as wine of beef and iron or other N. F. formulas, he must either amend his bond for the withdrawal of non-beverage alcohol or file a new bond that will cover wines for such purpose as well as alcohol.

The pharmacist must, however, bear in mind that this decision

does not cover the dispensing of potable distilled spirits or wines as medicines even when sold legitimately on prescription. The following Regulation of the Internal Revenue Department, promulgated June 30, specifically applies to the sale or dispensing of distilled spirits or wines for medical uses.

TO COLLECTORS OF INTERNAL REVENUE AND INTERNAL REVENUE AGENTS IN CHARGE:

Section 1 of the Act of November 21, 1918 (War Prohibition Law), provides that after June 30, 1919, until the conclusion of the present war, and thereafter until the termination of demobilization, the date of which shall be determined and proclaimed by the President, no distilled spirits held in bond shall be removed therefrom for beverage purposes, except for export; also that no beer, wine or other intoxicating or vinous liquors shall be sold for beverage purposes, except for export. It authorizes the Commissioner of Internal Revenue, with the approval of the Secretary of the Treasury, to prescribe rules and regulations regarding the manufacture and sale of distilled spirits and removal of distilled spirits held in bond for other than beverage purposes, and to govern the manufacture, sale, and distribution of wines for sacramental, medicinal, or other than beverage uses.

In view of these provisions and of the further fact that the Commissioner has jurisdiction under the general revenue laws over spirits and wines on bonded premises and withdrawals from bond for export, the following instructions are issued:

EXPORTS.

The existing regulations governing the export of wines tax free (T. D. 2416 and 2505), and governing the export of spirits free of tax or with benefit of drawback (Regs. No. 29), will continue in force and effect for the export of wines or distilled spirits during the war prohibition period.

If circumstances arise in connection with such exports to which the regulations seem inapplicable, or which they do not fully provide for, all such circumstances should be submitted for specific ruling.

MEDICAL USES OF WINES AND SPIRITS.

Physicians may prescribe wines and liquors, for internal use, or alcohol for external uses, but in every such case each prescription



shall be in duplicate, and both copies be signed in the physician's handwriting. The quantity prescribed for a single patient at a given time shall not exceed one quart. In no case shall a physician prescribe alcoholic liquors unless the patient is under his constant personal supervision.

All prescriptions shall indicate clearly the name and address of the patient, including street and apartment number, if any, the date when written, the condition or illness for which prescribed, and the name of the pharmacist to whom the prescription is to be presented for filling.

The physician shall keep a record in which a separate page or pages shall be allotted each patient for whom alcoholic liquors are prescribed, and shall enter therein, under the patient's name and address, the date of each prescription, amount and kind of liquors dispensed by each prescription, and the name of the pharmacist filling the same.

Any licensed pharmacist or druggist may fill such prescriptions (1) if his name appears on the prescription in the physician's handwriting, and (2) if he has made application and received permit, Form 737, in accordance with the provisions of T. D. 2788, and (3) if he has qualified as retail liquor dealer, by the payment of special tax. No such prescription may be refilled.

Druggists filling these prescriptions shall preserve in a separate, carefully guarded file, one copy of every prescription filled, and once a month shall transmit to the collector of internal revenue a list showing the names of the physicians, the names of the patients, and the total quantity dispensed to each patient during the month. These lists shall be subject to immediate examination and frequent review in the collectors' offices, and wherever there is indicated either (1) that a physician is prescribing more than normal quantities, or (2) that any patient, through the services of one or more than one physician, is procuring more than a normal quantity, the collector shall report the facts to the Commissioner and the U. S. Attorney.

Pharmacists should refuse to fill prescriptions if they have any reason to believe that physicians are dispensing for other than strictly legitimate medicinal uses, or that a patient is securing, through one or more physicians, quantities in excess of the amount required for legitimate uses.

Wholesale or retail liquor dealers having stocks of wines or liquors on hand, may sell to pharmacists holding permit, upon re-

ceipt of order on Form 739 and in conformity with the provisions of T. D. 2788, until their present supplies are exhausted. Such orders may be filled from spirits taxpaid at the \$6.40 rate.

Wholesale or retail liquor dealers who are not licensed druggists or pharmacists will not be permitted to qualify, after their present stocks are exhausted, to deal in either beverage or non-beverage spirits.

Wholesale pharmacists may continue to qualify for the sale of liquors or wines for non-beverage purposes, in conformity with the provisions of T. D. 2788.

Non-beverage alcohol, tax-paid at the rate of \$2.20 per gallon may be used in filling prescriptions for spirits or alcohol so medicated or denatured in accordance with existing regulations as to be unfit for beverage use. In filling prescriptions for spirits or alcohol not so medicated or denatured as to render it unfit for beverage use, liquor tax-paid at the rate of \$6.40 per gallon only must be used.

Tax-paid wine must be used in all cases.

#### SACRAMENTAL WINES PRODUCED UNDER CLERICAL SUPERVISION.

The procedure outlined in T. D. 2765 for the production of wines in quantities not exceeding 1,000 gallons should be followed where wines are produced for sacramental purposes by churches or religious orders, and the production and distribution is entirely under clerical supervision. Such wines may be removed from the premises where produced, in accordance with the provision of T. D. 2788. The labels required by that T. D. may be omitted.

The details of the procedure outlined in the two Treasury Decisions mentioned will be furnished to any interested person, by the collector of internal revenue for the district in which the wines are produced.

If objections are made to collectors that the provisions of the Treasury Decisions are inapplicable to the established procedure of any recognized religious body, and that they impede or interfere with historic rites or customs, the collector will carefully investigate the facts and make full report to the Commissioner in order that it may be determined whether the regulations should be modified to meet the needs of the particular case. Wine used for sacramental purposes is subject to tax.

### GENERAL INSTRUCTIONS.

All inquiries relating to the methods of shipping wines or spirits in filling non-beverage orders should be made to the local representative of the United States Railroad Administration.

The Department of Justice has exclusive jurisdiction to enforce the prohibition provisions of the Act of November 21, 1918 (War Prohibition Law). Accordingly it should be suggested to all persons making inquiry as to the prohibition provisions of the Act that they address either the Attorney General or the local United States Attorney. Similarly, when internal revenue officers become aware of apparent violations of the prohibition provisions of the Act, they should report such facts as come to their attention to the local officers of the Department of Justice. They will coöperate with the Department of Justice agents if such coöperation is requested.

The regulations and instructions regarding the use of non-beverage spirits and alcohol for purposes other than those specifically dealt with herein will continue in effect.

Where there is evidence that wine or liquor obtained actually or ostensibly for sacramental, medicinal, or non-beverage purposes has been used for beverage purposes it shall be reported to the Commissioner for assertion of additional tax liability, and to the United States Attorney for prosecution under the Internal Revenue laws.

So long as the taxes on alcoholic liquor and on occupations connected with the production and sale of alcoholic beverages remain in force they must be enforced. The Attorney General has advised this Department that the fact that an occupation or the production or sale of a beverage is prohibited does not relieve those engaged in such occupation of producing or selling the beverage from tax liability. It must, however, be clearly understood that payment of tax in no way conveys any right to act contrary to or to be exempt from liabilities imposed by the prohibition legislation. The result of the statutes imposing the taxes and prohibiting the traffic is that the same person may incur liability to tax and at the same time be liable to prosecution under the prohibition laws.

DANIEL C. ROPER,

*Commissioner of Internal Revenue.*

APPROVED:

CARTER GLASS,

*Secretary of the Treasury.*



There are several features of this regulation that call for comment. The pharmacist who desires to avail himself of this privilege must see that his bond given for *non-beverage* spirits and wines and the permit obtained covers the sale of such as medicines and on prescription and then *must again take out the objectionable tax stamp as a retail liquor dealer*, as if actually engaged in the sale of *beverage* liquors. Further, under the provisions of the Revenue Act of 1918, if he is engaged in such business in a state or district that is under prohibition legislation, in which the state act or local ordinance does not exempt the sale of liquors for medicinal purposes, then he must pay the special tax of \$1,000. In our opinion *no pharmacist in the discharge of his professional services in any community, will be warranted to pay \$1,000 for the right to dispense any or all classes of medicines*. The principle is absolutely wrong, ethical pharmacy should be totally divorced from the business of the liquor dealer and such has always been the contention of pharmacists.

It is observed that the regulations do not provide for the handling or supplying on prescription or otherwise of malted liquors and even if the requirements as stated are met and the R. L. D. stamp secured this carries with it no right to sell or dispense the so-called "extracts of malt," unless they contain not less than twelve per cent. of malt solids, until such time as by presidential proclamation the provisions of the War Prohibition Law shall be terminated.

G. M. B.

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## A STANDARD DOSAGE MEASURE.<sup>1</sup>

BY GEORGE M. BERINCER, PH.M.,

CAMDEN, N. J.

Accuracy in the compounding of medicines is a first principle instilled into the mind of a pharmacist, and so he realizes fully the importance of correct weights and measures. This is a matter that is now also receiving official attention in some of the states, where the scales, weights and measures of the pharmacists, the same as those of other merchants, are periodically inspected by a representative of the state or municipal department of weights and measures.

<sup>1</sup> Presented at the annual meeting of the New Jersey Pharmaceutical Association, Atlantic City, June 11, 1919.

While in the past the apothecary may have used graduated measures of variable shapes and with indifferent and inaccurate markings, today he is supplied by the manufacturers with "standard graduates" the shapes and graduation of which have been standardized with the coöperation of the United States Bureau of Standards and the use of which is already compulsory by statutes in some of the states.

Accuracy in the administration of medicines is equally as important as accuracy in their preparation. The physician calculates the amount of active medicament that he intends shall be given his patient in each dose of the prescription that he directs. To the trained physician the word dose has a well-defined meaning, namely, the right amount to obtain the desired effect, no more and no less. So it is evident that if too much be given untoward effects or undesirable reactions may result and that if too little be given there may be expected a failure to produce any effect. In either case, the intent of the physician may be nullified with detriment to his patient. It is the height of inconsistency to invalidate the judgment, the professional knowledge and skill of the physician and the pharmacist and to make these useless by the careless or inaccurate administration of the medicines.

The inaccuracy of the ordinary dose measures has been so frequently decried that the variability and uncertainty of these should be common knowledge. The almost universal custom is for the physician to direct as a dose of a liquid medicine, either a teaspoonful, a dessertspoonful, a tablespoonful, or possibly so many drops. Spoons of all sizes and shapes are marketed by the various manufacturers without any attempt to standardize the content of those bearing the same designation. In the same household one teaspoon may hold 55 minims and another as much as 80 minims and as great a range of variation may be shown by the dessertspoons and the tablespoons. Another source of error in measuring with the ordinary metal spoon, is what may be termed the personal equation. One person does not hold the spoon level, another gauges the spoon as full when it is not entirely filled. Even more uncertain and unreliable is the measurement of the fractions of the teaspoonful that are not infrequently prescribed for children. Although it is very generally conceded that the metal spoon of the household use is too uncertain and unreliable for the administration of medicine it, nevertheless, even at the present time, is the most commonly employed measure for this purpose.

To overcome the unreliability of the spoons, the glass manufacturers have placed upon the market medicine glasses and medicine goblets, of various shapes and sizes, marked for the measurement of teaspoonfuls, dessertspoonfuls, tablespoonfuls, etc. Unfortunately, the shapes selected have not been such as would permit of accurate measurement and in some cases the graduation has been very careless and inaccurate and the common medicine glass shows very little if any advantage in accuracy over the variable spoon. It is apparent that 60 minims of a liquid distributed over the bottom of a broad tumbler or goblet shaped vessel, will make so little showing that it will be difficult to gauge and to properly graduate this, and it will be impracticable to indicate lesser amounts.

The commonly employed medicine dropper for measuring medicines directed to be given in doses of so many minims or drops is likewise far from accurate. This can be readily demonstrated by measuring accurately the same number of drops of the same liquid as dropped by a number of these.

The physician has in mind a definite amount of liquid as the equivalent of the dosage term he uses. It is almost an invariable rule, that to him a drop is one minim, a teaspoonful is one fluidrachm, a dessertspoonful is two fluidrachms, a tablespoonful is four fluidrachms or a half fluidounce. Upon these equivalents he bases his calculations for the intended doses of the medicaments in his prescriptions. Practically all of the formulas in use by physicians and published in the works on medicine and the treatment of diseases, are based upon these commonly accepted equivalents, and these have also been generally employed in the "ready-made medicines" so frequently dispensed.

The United States Pharmacopœia IX recognized the seriousness of the prevailing inaccuracy in the administration of liquid medicines and while not adopting the suggestion that a standard form for a dosage measure should be defined, the Committee of Revision compromised by making in the "Introductory Notices" the following statement on page li.

#### "APPROXIMATE MEASURES.

"Physicians have hitherto very commonly prescribed liquid medicines in teaspoonful, dessertspoonful or tablespoonful doses. Inasmuch as spoons vary greatly in capacity, and from their form are unfit for use in the dosage of medicines, it is desirable that the



more scientific practice should be always adopted, of prescribing doses in mils, fluidrachms or minims, to be measured with a suitable medicine measure. The following are the values conventionally attached to the several approximate measures above mentioned:

“METRIC.

A teaspoonful	= 4 mils.
A dessertspoonful	= 8 mils.
A tablespoonful	= 15 mils.

“APOTHECARIES’ SYSTEM.

A teaspoonful	= 1 fluidrachm.
A dessertspoonful	= 2 fluidrachms.
A tablespoonful	= $\frac{1}{2}$ fluidounce.”

The use of the equivalents as stated in the Pharmacopœia has given entire satisfaction and their general acceptance indicates such a firm establishment that they should be permanently continued.

Doubtless if the Pharmacopœia had gone one step further and described “a suitable medicine measure,” the manufacturers of such wares would have adopted this as a standard and the uncertainty of the dosage of liquid medicines and the use of the unreliable spoons and medicine glasses, before this time, would have been largely curtailed.

The necessity for standardizing the measure as well as the equivalents of the doses in order that the uncertainty of the dosage of medicines may be terminated, is thus presented. It is not creditable to the medical profession and to the intelligence of this generation that the inaccuracy of the administration of liquid medicines has existed for so long a time and still less so that it be permitted to continue. The purpose of this communication is to present a study of this necessity that has led the writer to design a Standard Dosage Measure.

What are the essentials for such a measure? The *doses* that are commonly prescribed and which must necessarily be shown on the measure claim first consideration. Experience advises that these are certain numbers of standard drops or minims, such as 5, 10, 15, 20, 30; the teaspoonful, and at times fractions thereof, such as one-fourth, one-half; the dessertspoonful; the tablespoonful and occasionally the wineglassful. These with their metric equivalents it was concluded should be indicated upon the measure.



STANDARD DOSAGE MEASURE GLASS.

The *shape* must be such as will permit of the smallest of these named doses, 5 minims, occupying an appreciable space in the measure and also such that each of the doses named as necessary may be accurately measured and graduated. It must also be sightly and convenient to drink and to pour from. The inverted cone is the only shape that possesses all of these qualifications and so this form was adopted.

The *graduation* must be clear and accurate and indicate by distinct lines and lettering each denomination.

*Stability* is another essential so that the measure will not be easily upset. A relatively, broad, flat, round base was decided upon with a short heavy stem just above and the weight of glass at this point adds materially to this important feature.

The glass designed, as a result of this study, as the standard dosage measure is shown in actual size in the accompanying illustration and a sample is exhibited. It will be noted that it contains distinct graduations for 5, 10, 15, 20, 30, 45, 60 minims; the teaspoonful, and the one-quarter, one-half and three-quarter fractions thereof; the dessertspoonful; the tablespoonful; and the wineglassful along with their equivalents in mls. The denominations are arranged in three distinct columns under proper classifications. Each graduation is distinct and each dose, even down to the smallest indicated, 5 minims, can be accurately measured.

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## SECRET—PRIVATE—PERSONAL.

### No. III.—PERSONAL.<sup>1</sup>

By JOHN URI LLOYD, PHAR.M.,

CINCINNATI, OHIO.

*"Personal.* Of, or pertaining to a particular person; relating to, or affecting, an individual, or each of many individuals; peculiar or proper to private concerns; not public or general; as, *personal* comfort; *personal* desire."*—Webster.*

Wherever one turns eye or thought, comes to view a thing newly perceived or a thing recollected, to remind of something else. The leaf of this tree, the flower of that shrub, speaks relationship with

<sup>1</sup> For the prior papers of this series see AMERICAN JOURNAL OF PHARMACY, April and June issues.



others. The fragrance of this aromatic gum or resin reminds of another; the juice of this cane reminds of other sweets; the chewed leaf of acetocella, of other sours; a sliver of gentian brings to thought other bitters; the smoke of smouldering cascarilla reminds of musk. Indeed, a single substance may play a double part, as thought turns first to one substance and then to another. Close your eyes, warm the blossom of the sweet shrub in your hand, think of *strawberries*, then bring the blossom to your nostrils, the aroma of strawberries comes also. Think now of pineapples—behold, the same unweighable emanation from the same blossom, impresses the senses with the likeness of the delicious *pineapple*. The taste of dulcamara is first bitter, then comes the sweet after-taste—hence the well-applied name, “bitter sweet.”

Personal is each thing that is—and yet, no two leaves are exactly the same in contour, edge and thickness, no two odors are precisely alike, separated is each from the other, by some distinction, slight though it be. Although nature leans on the one-ness of the family relationships, inherent in its several parts, there are yet shadings bespeaking individual distinction. To level the whole by destroying the personality of each fragment in this mighty maze, would be untenable, unthinkable.

Akin to the modest violet, clinging close to the earth in the woodland's shadows, is the mighty hickory that, far separated by structure and nature, rears its head aloft and basks in the sunshine above its fellows of the primeval forest, looking down even upon the top of its sturdy oak companion. A cloak of bark has each trunk—that of the hickory shell-like, that of the oak deep-furrowed—the violet nestles perhaps in a crevice of the root bark.

Who would seek to endow the snow-white lily of the valley with the glory of the wild rose, or, because the lily, compared, for its beauty, with the splendor of Solomon, is white, would one take from the rose the blush of red that crowns its thorny stem? Who would drive from the dove its gentle personality, or make of the eagle a trembling nonentity? Wherever in air, liquid or earth man turns the critical eye, come family relationships, as well as individual distinctions, that teach him inclined to reason from the lesson nature spreads before him, that this mighty maze is not a disjointed medley, but a systematic whole, in which the greatest lessons, of strength, usefulness or beauty, may come from a study of the closest shadings that tend to personality.

Turn thought now to man, whose complicated accomplishments are cosmopolitan in the extreme. Restrict it to those concerned in the various sections of pharmacy. Should they be denied the right of personality? Instead, is not the field of him involved therein so great, in its recesses of observation, as well as research opportunities, that all-important to the world at large is *personality*? Is there not room for each individual to stand distinct as contrasted with others in his vocation? Does not the very acme of pharmacy's opportunity and service to humanity, as a whole, depend on the *quality* distinctions of her votaries?

Back, five decades and over, turns the thought of this writer, to where, in the commencement of his studies, behind the prescription counter, fifteen years successively, he stood a "druggist's clerk," aiming to qualify himself, as far as possible, in the art of pharmacy. To have suppressed the *personal* ego so earnestly encouraged by his preceptors, would surely have been to blast life's opportunity. And yet, it is plainly apparent that artificial, medico-pharmaceutical ethics of that period, indiscriminately illogical, were persistently endeavoring to suppress the individuality of pharmacists who, by studious effort leading to personal business opportunity, were seeking future professional recognition.

Who of that period cannot recall the "codists'" blanket efforts to prevent physicians from a right to direct a patient to a pharmacist possessing exceptional qualifications, in perhaps one phase of the art needed in a special compound? Who of those times cannot recall, not by innuendoes alone, but by open charges that *royalties* were paid physicians by the pharmacists who, by earned distinction, had the right to professional favors? Who of that period cannot bring to mind reflections cast on both the physician and the pharmacist, when a physician directed that a prescription be taken to a certain pharmacist whom the physician knew to have become qualified in some phase of the art, by experience as well as by special research?<sup>2</sup>

May we not individualize by citing a few examples from times gone by?

<sup>2</sup> That royalties were paid by some pharmacists to some physicians is not denied by this writer, who asserts, however, that such processes were never practiced by men classing with his preceptors or physicians favoring them with distinctive patronage.

• Prof. A. Fennel made himself a reputation, as a pharmacist, second to none anywhere. One of the specialties worked out by him for Dr. Williams, the famous leader of American eye specialists, was *brown citrine ointment*.<sup>3</sup> Dr. Williams knew from experience that, as made by Prof. Fennel, the substance, which for use in the eye needs be unquestioned, was exactly as it should be. And yet, were not innuendoes cast at those two conspicuous leaders in their respective professions? *The ethics of the levelers down* were being broken by this "partiality." Everyone knew that no risk was run when the label of the talented pharmacist, A. Fennel, was on that jar.<sup>4</sup>

Prof. Wm. B. Chapman, a pharmaceutical educator, experimented (1864–1865), in his modest little apothecary shop, until his pin-dipped gelatin capsules, pioneers at that date, attained a well-earned professional reputation, Cincinnati over. And yet, scarcely did a physician dare to specify "Chapman" on a prescription. At that date suppositories were made by pouring medicated cocoa butter into paper cones, each resting in the mouth of a wide-mouth vial. Chapman devised a metal mould, two sizes, one capable of making twelve, the other six suppositories. He experimented with excipients until he determined not only that an addition of ten per cent. of Japan wax improved the cocoa butter, but that different proportions were desirable with different drug admixtures. A great study did he make of suppository problems and distinction necessities.

Here, too, prevailing *ethics* tended to crush the personality of him who *knew* in pharmacy, by right of discovery and of persistent thought and experimentation, care and effort. Wrong was it for any but the most independent physician to give personal recognition to this man's distinctive qualification, in this specialty he had developed. Standing head and shoulders above all others in this field, for Chapman to have *advertised* either his gelatin capsules or his *suppositories* made by means of a mould he had devised, would have been to damn him ethically. In the case of this exemplary

<sup>3</sup> In this cod liver oil replaced neats-foot oil (U. S. P. 1850), then official in citrine ointment.

<sup>4</sup> Indeed, that fair-minded pharmacists recognized the justice of the case is evident, because "Gordon," with whom this writer was an apprentice, purchased the preparation from "Fennel," in order that Dr. Williams might have no reason for complaint.



man, such misapplied ethics, applied to the limit, kept him ever in commercial shadows, losing to him finally his loved pharmacy. Came the thought to this writer, in a final visit to Prof. Chapman's humble home, where lay this man of science, breathing his last—"If regularity in ethics brings to such as he neither personal opportunity, professional distinction, nor well-earned home comforts, such ethics is a misnomer. Better to live afar from the Code, contribute to humanity as an individual privileged to give or not, as seems proper, and die an *irregular*.<sup>5</sup>

Probably each reader of these lines engaged in prescription pharmacy half a century ago, in any American city, can testify to incidents paralleling such as this, incidents bespeaking the wrong resulting from a misapplied code aiming to *elevate* the many, at the expense of the few.

And what of the present? Let those concerned therein speak. They can answer the question as to how recognition is now given him who, in enthusiasm, devoted years to the study of the pharmacist's art, as contrasted with him who came into it for business only, from the outside, who never filled a prescription, never attended a college of pharmacy or served an apprenticeship, and yet blazes his name as pharmacist, close to his "cut rate" sign, and as the law permits, engages a "clerk."<sup>6</sup>

*A Plea for Justice.*—Is this writer alone, all alone, in asking that balanced thought be given the shortcomings of this great *ethical* problem that, founded on past altruistic ideals necessitated by deplorable abuses, stares the faces of those who to-day enter this field to study, work, sacrifice, in humanity's behalf? Is it possible that the young man who seeks to qualify himself above the multitude indifferent either to true ethics or earned service, seeking the opportunities given by our colleges of pharmacy, will forever be denied the *personal* recognition earned thereby? Is he forever to compete with commercial tradesmen—forever to be denied *personal* recognition, even by the profession of medicine? Is he, after his well-

<sup>5</sup> By right of experience do I write. After Dr. Chapman failed in business, for two years he was "head clerk" of Mr. Gordon's pharmacy. Under him an apprentice needed no incentive to master his art,—Dr. Chapman was an enthusiast, even in his misfortunes.

<sup>6</sup> Too well this writer appreciates that "cut rate" signs are not a monopoly of the pseudo-pharmacist. Nor are extravagant newspaper advertisements restricted to untaught physicians.

earned diploma is handed him, then to discover that his *personality* is to be suppressed, under the misapplied argument that one pharmacist is the equal of another—that he cannot assert his personal right to manipulative superiority? That all he evolves must be open to others—that he must needs, perhaps, give a gold mine to his advertising competitor, or a moneyed man's business investment? Is he forever to be governed by either a written or an unwritten code of laws that, formulated by men who make their living otherwise, has never harmonized, and never can harmonize, either with rules of business, precepts of law, or with commercial processes that govern the methods of men, the world over? Are the teachers in our colleges of pharmacy not to be encouraged in their great sacrifices, so that they may in some way reasonably assure their graduates that merited recognition will be given well-earned *personality*, whether they create a something new, or make a serviceable discovery touching medicines?

SUMMARY.—Take now the three words—*Secret*, *Private* and *Personal*. Draw better than this writer, if one can, a sharp distinction between each, as contrasted with the others. With these words, all differentiating shades of expression run into each other; with all, good or bad ethics may result, if respective definitions be inflexibly applied thereto.

May not this series of studies, based on a life-time spent in pharmacy, be considered as an attempt (very superficial) to do no more than lead modern thought in some way, to consider the possibility of giving both ethical credit and substantial return to the qualified pharmacist to whom such is due? That is, if any code other than a personal acceptance of "THE GOLDEN RULE," is really essential to life and action, either of persons engaged in the profession of medicine, or those concerned in the art of pharmacy.

# ON THE STABILITY OF DIGITALIS LEAF EXTRACTS. (FIRST PAPER.)

BY JAMES M. SCHMIDT AND FREDERICK W. HEYL,

KALAMAZOO, MICH.

Chemists have not yet succeeded in agreeing upon the chemistry of digitalis leaves and it is very probable that the question will remain unsolved until the fullest pharmacological assistance is brought into closest coöperation. A chemist in proceeding with work upon a lot of digitalis leaves ought to be informed upon the activity of the drug and of various extracts such as the water-soluble and water-insoluble parts; of the ether extract and of the chloroform extract of the water-soluble part. Before proceeding with the study of any one of these four fractions he ought to have a precise idea of what the relative toxicity of the fraction is, and also whether the fraction retains it without deterioration during the study thereof. Furthermore, he ought to be able to repeat the first extractions and purifications and arrive at definite crude fractions uniformly. The most significant advances might be made if the efforts of chemists were placed upon the production of the crude fractions of somewhat constant composition rather than upon the study of refined products of crude material which they either did not prepare themselves, or which they have not in the first place prepared repeatedly with some degree of uniformity.

Of the crude fractions which offer some hope of positive results we have above all the ether and chloroform extracts of the water extract. The water extract, however, has been prepared by different methods, and consequently the constituents of these extracts (with the possible exception of digitoxin) cannot be said to be understood.

Schmiedeberg<sup>1</sup> first described a substance designated as "digitoxin." The leaves were extracted with 50 per cent. alcohol, after a preliminary water extraction. The alcoholic extracts were clarified with lead acetate, filtered, and the filtrate freed from the excess of Pb with ammonia. After again filtering, the fluid was concentrated to remove alcohol. When the alcohol had been removed, a precipitate separated consisting of "digitoxin and fat, etc." This was washed with dilute soda solution, with water and dried. The dried residue thus obtained was extracted with chloroform.

<sup>1</sup> *Arch. f. Path. u. Pharm.*, 3, 16 (1874).



The chloroform was recovered and the residue digested with ether and petroleum ether. The insoluble crude digitoxin is recrystallized from 80 per cent. alcohol, from which it separated in fine needles or leaflets as a crystal powder, melting at about  $240^{\circ}$ .  $C = 63.6$ ;  $H = 8.5$ . It is insoluble in water, benzin, ether, cold alcohol, but more readily in hot alcohol, and very soluble in chloroform.

Kiliani<sup>2</sup> took up the work twenty-one years later. He followed Schmiedeberg closely as to extraction. He extracted first with water to which 5 per cent. alcohol had been added. The water extract was shaken with ether and the deep green extracts were shaken with dilute soda solution. As he now concentrated the ether solution, crusts separated, which were filtered off and washed with ether. The yield was 0.015 per cent. It was considered digitoxin but as it did not agree entirely with Schmiedeberg's it is designated as  $\beta$  digitoxin.

The same substance was isolated in larger quantity (0.085 per cent.) by extracting with 50 per cent. alcohol after first removing the water extract. The 50 per cent. alcoholic extract was precipitated with lead subacetate and filtered. Alcohol was recovered from the filtrate which was then exhausted with ether. The ether extract was washed with water. When concentrated, more " $\beta$  digitoxin" separated in crusts. This material was crystallized from 5-10 parts of boiling 85 per cent. alcohol, whereupon wartlike aggregates of leaflike crystals separated, melting at  $145-150^{\circ}$  and containing water of crystallization. When dissolved in methyl alcohol + chloroform (1:1) and crystallized by the addition of ether it separates in small prisms, water-free and decomposing above  $240^{\circ}$ .

Concerning the identity of  $\beta$  digitoxin with Schmiedeberg's preparation as well as with the product of Merck, Kiliani finally concluded<sup>3</sup> that these products were identical, and possessed the formula  $C_{31}H_{54}O_{11}$ <sup>4</sup>  $C = 63.9$ ;  $H = 8.5$ . The experimental work recorded is not conclusive in our opinion.

Kiliani in this work first hydrolyzed his  $\beta$  digitoxin with dilute hydrochloric acid and separated digitoxigenin. This body crystallizes from boiling 95 per cent. alcohol upon the addition of water in large prisms and does not melt at  $220^{\circ}$ . (Sinters at  $225-230^{\circ}$ .) This substance to which the formula  $C_{21}H_{32}O_4$  was first assigned is now corrected to  $C_{22}H_{32}O_4$ . The sugar split from digitoxin is digitoxose,  $C_6H_{12}O_4$ , m.p.  $101^{\circ}$ ,  $(\alpha_d) = +46^{\circ}$ . It is an interesting methyltetrose sugar. The presence of this sugar group causes the characteristic color test for digitoxin, *i.e.*, with  $H_2SO_4$  containing a trace of iron sulphate, a wine red coloration results. In hydrochloric acid a yellow color changing to green is obtained. Dissolved in acetic acid containing iron sulphate plus sulphuric acid containing iron, an indigo blue is obtained.

Although there was thus some agreement on this substance as an ether or chloroform extractable product, Kraft<sup>5</sup> has rather failed to confirm these views. Kraft extracted with cold water clarified with lead acetate and

<sup>2</sup> *Arch. d. Pharm.*, 233, 311 (1895).

<sup>3</sup> *Arch. d. Pharm.*, 234, 273 (1896).

<sup>4</sup> *B.* 31, 2454 (1898).

<sup>5</sup> *Arch. Pharm.*, 250, 118 (1912).

sodium phosphate, and precipitated all the products in the water extracts with tannin. From this he liberated the glucosides in the usual manner with ZnO. These were taken up as far as possible in water and the water solution was extracted with chloroform. The activity was in the chloroform extract while the water soluble substances which greatly predominated (5 per cent.) are saponins, which upon hydrolysis yield glucose and a pentose. Interest therefore centers in the chloroform extract, but at this point Kraft dropped the work and instead shook out fresh aqueous extracts with chloroform omitting the tannin procedure. From this chloroform extract he precipitated with ligroin a substance termed by him "gitalin" but which appears to be a mixture.<sup>6</sup> The yield is 0.7 per cent.

Now Kiliani<sup>7</sup> had stated that the digitalis leaf extracts which had been ether-extracted would yield when subsequently chloroform-extracted a second active substance, not digitoxin but "digitophyllin." Later<sup>8</sup> in reviewing digitalis chemistry he omits this substance from consideration.

Kraft continued his work by extracting the water-extracted leaves with 50 per cent. alcohol. This extract was clarified with lead acetate filtered and concentrated to a small volume in the presence of calcium carbonate. A heavy precipitate separated as with Schmiedeberg. The precipitate is washed with 2 per cent. soda solution and dried, and the dried precipitate is exhausted with chloroform, which dissolved a glucoside agreeing, but not conclusively, with digitoxin.

After exhausting the dry precipitate with chloroform Kraft boiled the residue with alcohol, and a glucoside, "gitin" yielding galactose on hydrolysis was isolated C = 52.2; H = 8.1.

It therefore appears that the chloroform soluble glucoside present in water solutions and in 50 per cent. alcoholic extracts is not definitely known, but there is a certain quite reasonable hypothesis that there is a chloroform soluble glucoside, yielding digitoxose on hydrolysis, and which is insoluble in water when once it has been separated to a certain degree of purity. To this substance the term digitoxin applies. What the composition of "gitalin" is has not been studied further except that when one purifies it further a part becomes insoluble in chloroform, ether and water. Merck<sup>9</sup> has found in producing digitoxin that a part of the glucoside originally taken out by means of chloroform becomes insoluble. Kraft designates his insoluble product "anhydrogitalin," a digitoxose glucoside and it appears to be a pure product.

On the whole the chemistry of these substances is in an unsatisfactory condition. When the leaves have been exhausted with

<sup>6</sup> Kiliani, *Arch. Pharm.*, 252, 13 (1914).

<sup>7</sup> *Arch d. Pharm.*, 235, 425 (1897).

<sup>8</sup> *AM. J. PHARM.*, 85, 223 (1913).

<sup>9</sup> *B.* 48, 334 (1915).

water and when this extract has been exhausted with ether and chloroform, a very considerable part of the glucosides remain soluble in water and not in chloroform or ether. Here is a part of the subject even less understood.

Keller<sup>10</sup> attempted to duplicate Kiliani's work on a small scale (20 Gm.) and obtain a quantitative estimation of "digitoxin" and thus arrive at a conclusion concerning the activity of the sample. The leaves were extracted with 70 per cent. alcohol, percolate concentrated, precipitated with lead acetate, filtered, and excess of lead removed with sodium sulphate. The clear fluid is rendered ammoniacal and extracted with chloroform. These extracts are concentrated, redissolved in 3 Cc. chloroform and precipitated with an ether + ligroin mixture. This precipitate is weighed and calculated as digitoxin. Yield 0.26–0.62 per cent.

To illustrate the futile nature of Keller's assay we give an experiment wherein the activity of the "crude digitoxin" amounted to only 12 per cent. of that of the drug.

A tincture of digitalis U.S.P. (D-1625) was assayed by the one-hour frog method. Found M.S.D. = 0.0052 Cc.

Assayed by Keller's process the total crude chloroform extract (12 Gm. drug) weighed 73.1 Mg. = 0.6 per cent. Redissolved and precipitated with ether + ligroin the "crude digitoxin" weighed 48.4 Mg. (0.4 per cent.).

This was dissolved in 200 Cc., 70 per cent. alcohol. Forty Cc. (2.4 Gm. drug), was concentrated on the steam bath to remove alcohol, and then made up to 20 Cc. with physiological salt solution. (Solution =  $\frac{\%}{100} \times$  tincture strength.) M.S.D. = 0.0366 Cc.<sup>11</sup> The proportionate toxicity of Keller's "crude digitoxin" is therefore about 12 per cent. of the total of this drug.

We did not carry this work any further, as it has already been shown by Barger and Shaw<sup>12</sup> that the digitoxin isolated in Keller's process represents from 29 per cent. to 14.5 per cent. of the activity of the drug. This has also been established by Focke and others, and the proof is established that the chemical process above described is entirely useless.

The interest in Keller's work, however, accentuates the value of pharmacological work to chemical investigation. It is evident that a large part of the active substance or substances are either (a) lost in the resinous precipitate and lead acetate precipitate or (b) con-

<sup>10</sup> *B. d. d. Pharm.*, G. 7, 125 (1897).

<sup>11</sup> Equivalent to 0.018 Mg. p. Gram frog Keller's "digitoxin" *i.e.*, 0.5 Mg. for 30 G. frog.

<sup>12</sup> *Pharm. J.*, 73, 259 (1904).



tained in the aqueous liquor from which the "digitoxin" has been extracted with immiscible solvents.

Keller was the first to point out that he could obtain heavy precipitates in the extracted fluid with tannic acid after having exhausted the ammoniacal liquor with chloroform. It is now well understood that the leaves contain a water soluble glucoside or mixture of glucosides, and while it is not known how far the precipitation of resin removes activity it is suspected that a greater proportion of the activity of the leaf is water soluble and not found in the "digitoxin" shake out. This hypothetical substance is known as "digitalein."

Kilaini<sup>13</sup> and Windaus have made some observations on this point.

They prepared an infusion (15 minutes) which was concentrated with some loss of activity to a syrup. This was diluted with strong alcohol and the precipitate filtered off. The concentrated filtrate was dissolved in water and precipitated with tannic acid. The precipitated tannates were decomposed with zinc oxide and the liberated glucosides were dissolved in alcohol (4 parts). To this two parts of ether were added, and an active precipitate obtained (2 Mg.). It weighed 16 Gm. from 10 Kg. and was water soluble. To the main alcohol + ether solution, a further addition of ether (4 parts) gave a second precipitate which was water soluble and active (1 Mg.). The final solution from the ether precipitations contained 20 Gm. of which 2 Gm. was water soluble and toxic.

Kiliani then took the leaves which had already been used to prepare the infusion and extracted them with alcohol. The alcohol was distilled off, and the residue taken up with absolute alcohol and filtered. The alcohol was again removed from the filtrate and the residue taken up in water, and filtered from resin. This aqueous solution was extracted with ether and with chloroform. The water soluble part (1.5 per cent.) was very active (1.5 Mg.). The solution was saturated with magnesium sulphate and an active substance (0.6 Mg.) precipitated.

While the above work is chemically indefinite it is necessary to understand that it is from this work that the term "digitalein" is derived and that it means the water soluble active principle or principles of the leaf.

The work of Kraft also has a bearing on the water soluble constituents. Kraft it will be recalled first extracted the drug with *cold* water, and then after clarifying with lead and sodium phosphate, precipitated glucosides with tannin. This precipitate contained chloroform soluble material which was removed by extraction and also water soluble material which Kraft named digitalis leaf "saponin." Contrary to Kiliani's work on the infusion where an active "digitalein" was found, Kraft found his water soluble material

<sup>13</sup> *Arch. Pharm.*, 237, 464 (1899).

inactive. Kraft hydrolysed this saponin and detected by their osazones, glucose and arabinose (or xylose).

Kraft then reextracted his leaf with 50 per cent. alcohol and on removing the digitoxin as above described found that a hot alcohol extraction subsequent to the chloroform extract yielded "gitin" a crystalline galactoside, insoluble in water and in chloroform, melting at 260–265°. It crystallizes in needles and contains 11.5 per cent. water of crystallization.

The experimental work reviewed agrees in that a 50 per cent. alcoholic extract is found to yield more active extracts than a preliminary water extract. For example, Kiliani and Windaus made an infusion (10 Kg. leaf), from which 190 Gm. of tannate was precipitated, while a subsequent 50 per cent. alcohol extraction yielded after removing certain fractions with absolute alcohol, chloroform and ether, 150 Gm. of very active water soluble material containing "digitalein." This matter is very puzzling in view of the fact that we consider a fresh 10 per cent. infusion as practically equivalent to a 10 per cent. tincture when examined by the one-hour frog method. Work on this point, and on the rate of deterioration of infusions is in progress in this laboratory. Focke<sup>14</sup> states that the water extracts about 80 per cent. of the activity. Concerning the rate of deterioration of the infusion, results are very contradictory.

Several recent observations<sup>15</sup> have indicated that alcoholic extracts are not stable. This finding is of the utmost importance in therapy, and a clearer understanding of these values is important with reference to the chemical investigation of digitalis leaf. One of the most interesting points in this connection would be to observe whether or not these solutions finally arrived at a permanent equilibrium as to toxicity, and to observe what part of the toxicity was thus found to be stable. A chemical study of a digitalis extract aged in this manner would certainly be a more hopeful one to begin with. Is, for example, the permanent toxicity of an aged tincture the water-soluble fraction or is it the "digitoxin"? Or do we have a mixture of cleavage products? A series of examinations on samples of alcoholic extracts which we report below prove that a condition of greater stability is obtained on aging. These results are discussed in the summary at the end of this paper.

<sup>14</sup> *Arch. Pharm.*, 249, 323 (1911).

<sup>15</sup> Roth, *Bull. Hygienic Lab.*, 102 (1916); Pittenger & Mulford, *J. AM. PHARM. A.*, 7, 236 (1918).

EXPERIMENTAL.

*A. Tincture 1.* No. 35337 (D-1625) 2-15-17. A standard U. S. P. tincture, alcohol=64 per cent.

Date.	M. S. D., Mils.	Toxicity, Per Cent.	Period in Months.
Mar. 2, 1917.....	0.0061	100	
Apr. 20, 1918.....	0.0108	55	13
Jul. 20, 1918.....	0.0107	55	16
Aug. 17, 1918.....	0.0125	48	17
Sep. 1, 1918.....	0.0140	42	18
Oct. 12, 1918.....	0.0162	37.5	19
Nov. 3, 1918.....	0.0150	40	20
Dec. 1, 1918.....	0.0162	37.5	21

*Tincture 2.* No. 36498 (D-1625) 6-13-17. Alcohol=64 per cent. Assayed as follows:

Date.	M. S. D., Mils.	Toxicity, Per Cent.	Period in Months.
June 19, 1917.....	0.0060	100.0	
July 21, 1918.....	0.0120	50.0	13
Aug. 17, 1918.....	0.0150	40.0	14
Sept. 15, 1918.....	0.0160	37.5	15
Oct. 13, 1918.....	0.0160	37.5	16
Dec. 23, 1918.....	0.0160	37.5	18
April 1, 1919.....	0.0160	37.5	22

*Tincture 3.* Fat free. No. 37798 (D-1625) 1-10-18. Alcohol=46 per cent.

Date.	M. S. D., Mils.	Toxicity, Per Cent.	Period in Months.
Jan. 12, 1918.....	0.0060	100.0	
July 27, 1918.....	0.0093	64.0	6
Aug. 31, 1918.....	0.0120	50.0	7
Sept. 28, 1918.....	0.0150	40.0	8
Oct. 20, 1918.....	0.0160	37.5	9
Nov. 17, 1918.....	0.0160	37.5	10

*Tincture 4.* No. 38182 (D-1625 + D-460) 1-31-18. Alcohol=64 per cent. This tincture when first prepared showed a strength of 170 per cent. which was reduced to 110 per cent. by dilution.



Date.	M. S. D., Mils.	Toxicity, Per Cent.	Period in Months.
Feb. 9, 1918 . . . . .	0.0055	110.0	
July 27, 1918 . . . . .	0.010	60.0	5
Aug. 31, 1918 . . . . .	0.011	54.0	6
Sept. 26, 1918 . . . . .	0.0141	42.5	7
Oct. 20, 1918 . . . . .	0.0141	42.5	8
Nov. 17, 1918 . . . . .	0.0141	42.5	9
April 1, 1919 . . . . .	0.0141	42.5	14

Tincture 5. No. 39220 (D-1625) 6-21-18. Alcohol 64 per cent.

Date.	M. S. D., Mils.	Toxicity, Per Cent.	Period in Months.
June 29, 1918 . . . . .	0.0066	90	
July 27, 1918 . . . . .	0.0071	84	1
Aug. 31, 1918 . . . . .	0.00769	78.0	2
Sept. 28, 1918 . . . . .	0.00774	77.5	3
Oct. 20, 1918 . . . . .	0.00827	72.5	4
Nov. 17, 1918 . . . . .	0.00827	72.5	5
Feb. 23, 1919 . . . . .	0.00857	70.0	8

From these results we may plot the rate of deterioration for tinctures as recorded by the one-hour frog method as follows:

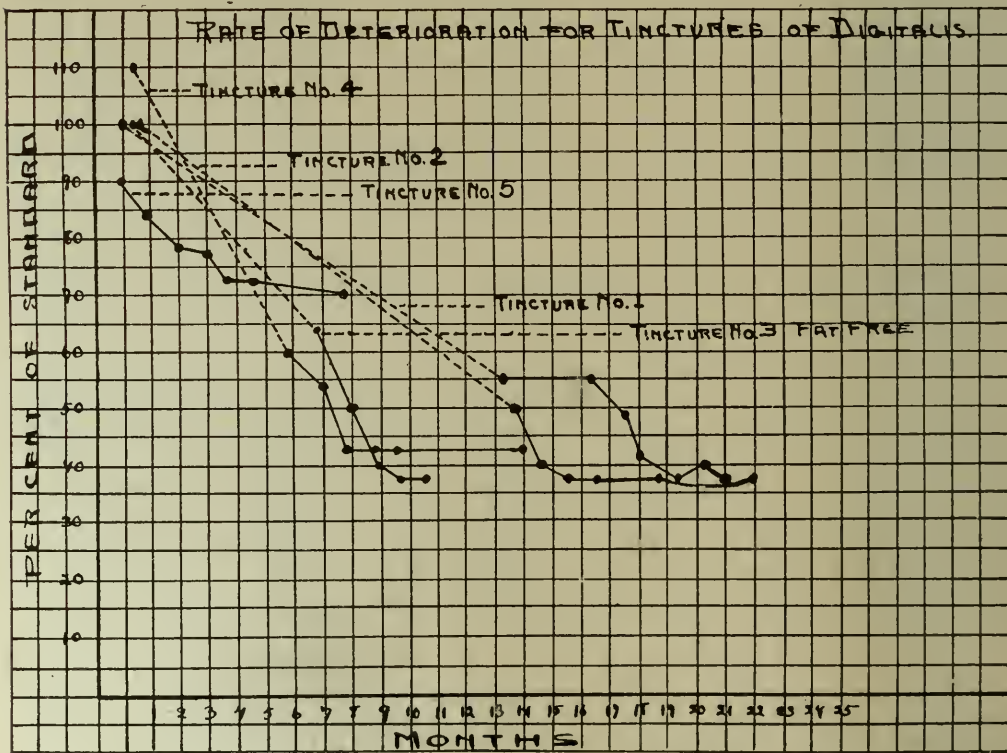


FIG. I.

*B. Fluidextract 1.* No. 36113 (D-1625) 5-10-17. Alcohol 75 per cent.

Date.	M. S. D., Mils.	Toxicity, Per Cent.	Period in Months.
May 11, 1917.....	0.000476	128	
Aug. 3, 1918.....	0.001153	52	15
Sept. 5, 1918.....	0.001260	47.5	16
Oct. 13, 1918.....	0.001260	47.5	17
Dec. 15, 1918.....	0.001260	47.5	19
Apr. 1, 1919.....	0.001333	45.	23

*Fluidextract 2.* No. 36113 (D-1625) as marketed, the preceding sample being diluted. Alcohol 75 per cent.

Date.	M. S. D., Mils.	Toxicity, Per Cent.	Period in Months
May 12, 1917.....	0.00060	100	
July 20, 1918.....	0.00143	42	14
Sept. 15, 1918.....	0.00160	37.5	16
Nov. 3, 1918.....	0.00150	40	18
Mar. 24, 1919.....	0.00150	40	22

*Fluidextract 3.* No. 37799 (D-1625)—the undiluted fluidextract before dilution for market. Fat free, about 50 per cent. alcohol.

Date.	M. S. D., Mils.	Toxicity, Per Cent.	Period in Months.
Jan. 12, 1918.....	0.000530	113	
July 14, 1918.....	0.000660	91	6
Aug. 6, 1918.....	0.000807	74	7
Sept. 5, 1918.....	0.001000	60	8
Oct. 13, 1918.....	0.001043	57.5	9
Oct. 27, 1918.....	0.001090	55	10
Jan. 19, 1919.....	0.001090	55	12

*Fluidextract 4.* No. 38459 (D-1625) as submitted for assay before final concentration.

Date.	M. S. D., Mils.	Toxicity, Per Cent.	Period in Months
April 9, 1918.....	0.000785	76	
July 13, 1918.....	0.000866	70	3
Aug. 10, 1918.....	0.000900	66	4
Sept. 8, 1918.....	0.001090	55	5
Oct. 12, 1918.....	0.001090	55	6
Oct. 27, 1918.....	0.001090	55	7
Jan. 5, 1919.....	0.001090	55	10
April 1, 1919.....	0.001142	52.5	12

The results are plotted upon the following chart:

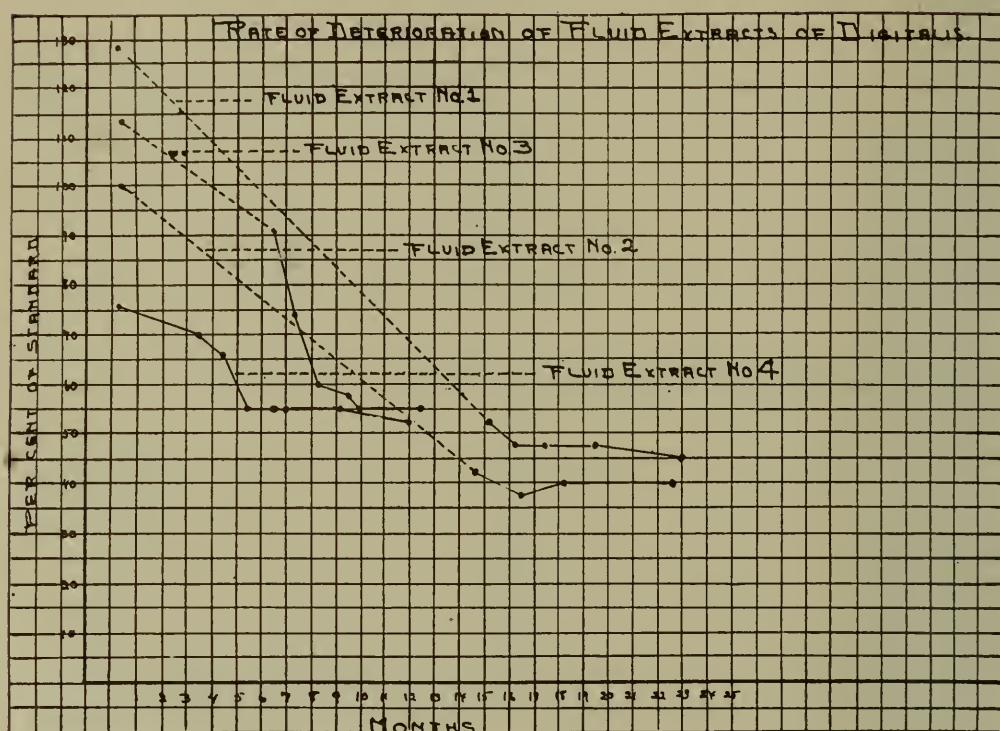


FIG. II.

*C. Stability of Dry Leaves.*—From these results given for tinctures and fluid extracts, the permanency of the drug as compared to the extracts may be plotted. Reviewing the above data with this in view we find that Drug D-1625 showed the following values:

Date.	Material Analyzed.	Drug Strength, Per Cent.	Age in Months.
Dec. 5, 1916 .....	(sample)	120	?
Feb. 15, 1917 .....	20 gal. Tinct.	150	
Mar. 1, 1917 .....	20 gal. Tinct. F. F.	136	
June 13, 1917 .....	20 gal. Tinct.	130	6 (in stock)
Jan. 12, 1918 .....	40 gal. Tinct. F. F.	100-113	13 " "
June 29, 1918 .....	20 gal. Tinct.	90	19 " "
Sept. 4, 1918 .....	40 gal. Tinct. F. F.	60	22 " "

Comparing the strength of fluid extracts prepared during the same period and from the same drug we have about the same curve.

Date.	Flex. No.	Drug Strength, Per Cent.	Age in Months.
May 10, 1917 .....	36113	128	5
Jan. 12, 1918 .....	27799	113	13
Apr. 9, 1918 .....	38459	76	16
Apr. 1, 1919 .....	sample of drug	50	28



The curves are plotted as follows:

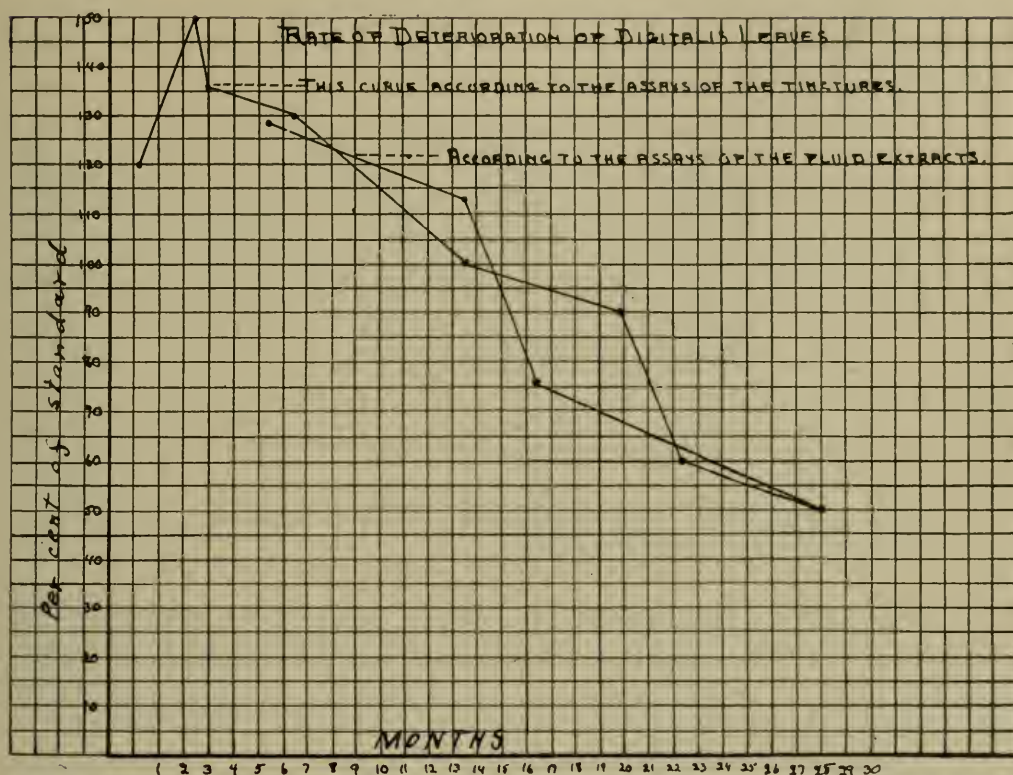


FIG. III.

### SUMMARY.

1. Alcoholic extracts of digitalis leaves, as well as the leaves themselves, gradually lose part of their activity; the losses in the extracts from young drug were irregular and the velocity of this reaction in alcoholic solution was much greater than in the drug itself.

2. An equilibrium of somewhat marked stability results, indicating that the leaf contains a constituent much more stable than a second active but unstable constituent which is also present.

3. In the leaf studied the more stable component represents less than half the total activity of the young dried leaf (40 per cent.). The results obtained on extracts made from older drug indicate (but not conclusively) that the drug, having lost more or less of the unstable active component, yields an extract which naturally comes to equilibrium, at a greater activity, owing to the predominance of the more stable constituent. This is conspicuously shown in Fluid-extract 4, where a rundown drug at least 16-18 months old (76 per

cent.) yielded an extract which came into equilibrium with 52/76 or 69 per cent. permanent activity. The following table summarizes the work in respect to this point, Tincture 5 being out of order and possibly not yet at equilibrium.

Sample.	Activity of Drug.	Gm. Drug in 1,000 Cc. Activity = 100.	Activity = 100.		Calculated Per Cent. Stable in 100 Per Cent. Activity.
			Per Cent. Stable.	Per Cent. Lost.	
Tinct. 1 .....	135	74	37.5	62.5	
2 .....	130	77	37.5	62.5	
3 .....	{ 100	{ 100	37.5	62.5	(51
	{ 113	{ 89			(45
5 .....	90	111	81	29	56
F. E. 1 .....	130	770	37	63	
2 .....	130	770	40	60	
3 .....	113	885	49	51	45
4 .....	76	1,320	69	31	67*

\* Leaf is at least 18 months old.

4. The above conclusions may agree with the hypothesis that "digitoxin" is the stable and that the so-called "digitalein" is the less stable part, the equilibrium point corresponding roughly with the percentage of "digitoxin" often found.

5. This work indicates the futility of conclusive pharmacological work on Galenical digitalis preparations and certainly points out a very good reason for the failure of pharmacologists to agree among themselves on many points.

The authors wish to expressly indicate that the above work was carried out incidental to the commercial production of the products and that further experimental work involving temperature control, percolation on smaller scale, etc., is desirable. The results are published as they clear up somewhat the very conflicting views found in the literature and in the profession, concerning the stability of this important drug.

RESEARCH LABORATORY, THE UPJOHN COMPANY,  
KALAMAZOO, MICHIGAN, May 2, 1919.

## THE CULTIVATION OF AROMATIC PLANTS IN THE UNITED STATES.<sup>1</sup>

BY P. H. TODD,  
 KALAMAZOO, MICH.

The lessons of the Great War have taught us, among other things, the dangers of relying on foreign resources for the important drug, dye and chemical materials on which many of our important industries depend. Happily for the perfume industry, the districts in which the production of aromatic oils is chiefly centered (southern France, northern Italy and Switzerland) remained in friendly hands and the supply of flower oils was not cut off. But though we hope that these districts, which our arms have helped to protect, will be forever free from the ravages of war, there will always seem to be a danger, while Europe remains in its present unsettled condition, that international complications may suddenly cut off the foreign and, at present, only source of supply of many of the most important perfume materials.

For this reason it is of interest to us to briefly review the extent of the volatile oil industry as at present developed in this country and to consider the possibilities of its further development with a view to our securing a fair measure of independence of the foreign sources.

The principal volatile oils produced in the United States are peppermint, spearmint, pennyroyal, wintergreen and sweet birch, sassafras, wormwood, tansy, erigeron, and the spruce, cedar and pine oils. Our production of these oils is not only sufficient for our own needs, but permits a large exportation to foreign countries. In the case of peppermint, about nine tenths of the total world's supply is produced in a few counties of southern Michigan and northern Indiana. Fifty years ago the chief source of this oil was in a few counties of England, Mitcham County among them, which gave its name to the variety most widely cultivated in this country. The development of the culture in this country has caused the perfection and adoption of more economical and efficient methods of production, so that in normal times this oil is produced much more cheaply here than in England.

<sup>1</sup> Address delivered at the annual convention of the Manufacturing Perfumers' Association of the United States.



A detailed discussion of the methods of producing these well-known oils will probably not be of sufficient interest to the perfume trade to justify its repetition here, the subject having been repeatedly covered in trade journals and technical books. It may be opportune, however, to mention the case of peppermint oil as an instance of the American tendency to simplify foreign methods of production when once established in an industry that was formerly confined to European countries. In England the peppermint roots or rhizomes are allowed to sprout in the spring, and when the sprouts have developed into plants two or three inches high these plants are separately set in the ground at regular intervals, thereafter being cultivated entirely by hand. In America the roots are laid in longitudinal trenches three feet apart and the cultivation is done with horses, both planting and cultivation being much cheaper this way. The English yield averages about fifteen pounds to the acre, whereas ours is usually not less than twenty-five, and often much more. When the crop is harvested, they distil theirs over boiling water, several hours being necessary for the complete distillation of one vat-full. We distil ours with live steam and a much larger vat-full requires only twenty minutes time in a modern still.

Of the oils which we secure chiefly from European sources the most important to the perfume trade seem to be lavender, rose, rosemary, geranium, neroli, orris root, and the flower odors isolated by the enfleurage or maceration processes, as jasmine, tuberose, violet, jonquil, hyacinth, etc.

The first of these, lavender, which is grown extensively in the mint-producing districts of England, has been successfully grown experimentally in Michigan where the Mitcham peppermint is so extensively grown. The only serious difficulty that presents itself is due to the frequent occurrence of heavy snows which tend to break down the bushes. Lavender is grown preferably in nicely rounded, compact bushes, and the flowers are cut off by grasping a handful of twigs at once and cutting them off together, with a sickle. Heavy snows flatten the bushes out, making the gathering of the flowers more difficult. However, this is not a prohibitive difficulty. There are localities in the Carolinas and other parts of the country where lavender could be grown with no climatic difficulty.

The distillation of rose has never been extensively undertaken in this country. In California, where the rose grows so prolifically, the atmosphere is probably too dry for a sufficient oil yield. It is

essential that the air be sufficiently humid so that there will be moderate dews during the harvesting season, as roses gathered in the morning, with a moderate dew upon them, yield a greater quantity of oil. In southern France the heat is rather too intense and the dews and rains are somewhat excessive. The production is carried on extensively there, however. In Bulgaria the conditions of soil and climate are very ideal. The mountains to the north shield the Bulgarian fields from the icy northern winds of the winter season, and the soil is largely old lake bottom of a semi-clay character, holding plenty of moisture but allowing an excess of it to pass through.

It seems improbable that the northern states can provide a suitable home for rose culture, but the ideal climatic and soil conditions can probably be approached closely south of the Mason and Dixon line and east of the Mississippi.

Rosemary oil, which is produced chiefly in Spain and along the Dalmatian coast, though it is raised quite extensively in England, but with greater difficulty, could probably be grown with excellent success in Florida. Rosemary needs a warm climate and should be grown on a dry, chalky soil, sheltered from cold northern winds.

Geranium oil is produced most successfully in the mild climate of Spain, and though it probably could not be successfully raised in the northern states, the southern states and California undoubtedly furnish favorable opportunities for its culture.

Oil of neroli, which is obtained from the flowers of the bitter orange, is distilled principally in southern France. Like geranium and rosemary, it probably could be produced with equal ease, as far as climatic and soil conditions are concerned, in the southeastern states.

Orris oil, from which irone is obtained, and which is distilled from the rhizome of the white flag, is obtained most successfully on a dry, strong soil with plenty of sun, and, with plenty of water available, the climate of California appears to be well suited to its production. The white flag has been grown there experimentally with good results.

The preparation of flower concretes and absolutes from the hyacinth, tuberose, jasmine, violet, jonquil, etc., has never been undertaken in this country on a commercial scale, though it seems very safe to say that they could be produced as well here as abroad excepting for the single element of labor. Experimental work in the

cultivation of these flowers for their essences is being conducted now by the Department of Agriculture, and also in the experimental gardens of the A. M. Todd Company at Mentha, Mich., and it is hoped the valuable information will be available from both sources within a year or two. It may be of interest to recall that in 1914 there were about 10,000 acres of hyacinths under cultivation in Holland in soils very similar to the black soils of the mint-producing districts of Michigan, these hyacinths being grown for the double purpose of extracting the perfumes, and the production of bulbs for market. Volatile solvents are used in extracting the perfume, this being the only method that has proven practicable.

To sum up the prospects for home-production of the important perfume materials, it would seem safe to say that in our vast country, with its variety of climates—hot, cool, dry and humid—and its endless variety of soils and geological formations, a suitable combination of soil and climate can be found for every perfume-bearing plant of present importance to the trade. The one single determining factor that will make successful culture of the plants possible or impossible seems to be the element of labor. The cultivation of aromatic plants entails a great amount of hand labor, and it appears that the success of the industry will chiefly depend on the relative labor cost here as compared with the cost of labor abroad, and the extent to which the greater cost here is offset by a moderate tariff, and by a liberal spirit on the part of the consumer of these materials, evidencing itself in a desire to give the preference to the home product when he finds it in competition with the foreign product; and even, if need be, in a willingness to pay a little more than the foreign price and so share a part of the burden, if, during the first few years, it is impossible, on account of abnormal labor cost or other causes, for the American producer to meet the foreign price without loss. Once this industry is fairly started, it is reasonable to believe that American genius will triumph over the difficulties that now present themselves, and that the American branch of the industry will be able to hold its own in the American market without further help from the consumer.

What seems to be rather an analogous case is the development in this country, during the last four years, of the cultivation of medicinal herbs, and especially of the important drug plants, belladonna and henbane, or hyoscyamus. Before the outbreak of the war, our requirements in the herbs were obtained entirely from cen-



tral Europe, so that the supply was abruptly and completely cut off. So dependent had we been on the foreign product that we not only were producing no herb, but had no seed. Fortunately it was possible to obtain a little of the belladonna seed from Scandinavia, and a small amount of the henbane seed had been saved at Mentha, from plants grown in the experimental garden. These seeds were planted, and very careful attention to the growing plants yielded an excellent quality of herb, though at a production cost that was several times greater than the usual market price before the war. Scientific study, however, has enabled us to rapidly cut the cost of production, in spite of the steady increase in the cost of labor, and as the American product is much superior in quality to the foreign herb, we are confident of our ability to continue permanently to meet foreign competition in this item. The success with henbane brought particular satisfaction, as it is an unusually delicate plant.

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## ADVERTISING.<sup>1</sup>

By JACOB DINER, PH.G., M.D.,

NEW YORK.

Funk and Wagnall's Dictionary defines the word "advertise" as follows: To make known; publish abroad; commend to the public. To my mind the more important part of the above definition is to "commend to the public." For after all, the essential object of an advertisement, speaking in the commercial sense, is to sell goods or services.

Now the mere publication of one's willingness to sell, barter or trade does not carry within itself any persuasion or argument to create in the reader of the "ad" the desire to purchase from or to deal with the advertiser. There must be something to recommend this particular store, merchandise or service to the would-be purchaser in preference to other similar offerings. Therefore an advertisement must commend, *i. e.*, it must be so designed as to convince the beholder not only of the desirability to purchase but to the absolute advantage of purchasing it from that particular seller or store.

<sup>1</sup> Read at the annual meeting of the New Jersey Pharmaceutical Association, Atlantic City, June 11, 1919.

Turning our attention to the various methods of advertising, we find that the majority of people limit themselves to newspapers, programs, circulars, placards and widow displays. To the average pharmacist, especially in the larger cities, newspaper advertising is not only prohibitive because of its expense, but is actually useless because of the fact that he has to pay for large circulation in order to reach a relatively limited few within his business radius.

It is not my intention at this time to enlarge upon the advantages or disadvantages of newspaper advertising, nor will I take up those other forms of advertising which involve an outlay of money. These methods are valuable and when properly employed are bound to yield rich returns.

I shall limit myself to that class of advertising which is practically free from expense, readily at the disposal of every pharmacist, and which not only is sure to yield a rich harvest in direct returns but which also has cumulative effect, bringing, as it were, compound interest. We can classify these methods under four main headings: (1) show windows, (2) arrangement of the store interior, (3) personal, that is individual, direct advertising, (4) service.

A casual glance at the average drug store window will convince the observer that pharmacists, with very few exceptions, are philanthropists of a high order. Is there anyone in this audience who is willing to contradict me when I say that any man is a philanthropist who spends at least 25 per cent. of annual store rental for the noble purpose of helping along the poor (?) and deserving (?) manufacturer of proprietary medicines?

It is true that in return for the use of your store window and store front, the manufacturer is kind enough to supply you with the dummies and signs for display, and will even go as far as allowing you to make a 10 per cent. gross profit, occasionally, on his goods, provided you buy enough at one time to last you forever and a day, and provided also that your neighbor on the next corner does not get ahead of you and bestow upon the dear public that 10 per cent. gross, which means about 15 per cent. minus, in order to create the impression that you are a highway robber.

There are many articles in the store which readily lend themselves for window display purposes. Every pharmaceutical journal has published volumes of information on that subject, and I shall

therefore merely call your attention to this phase of inexpensive advertising and leave it with you as a thought to take home as a "convention souvenir."

*Store Arrangement.*—The primary object of shelves, I suppose, was for the purpose of storing or keeping goods. The modern merchant, that is the successful one, however, is not so much concerned with keeping, as he is with selling the goods. Therefore the arrangement in the store should have that object in view and should be carefully planned and executed. You sell stamps, have a telephone booth or two, keep a directory more or less new, and offer other inducements to the passerby or to your neighbor to come into your store. But lest perchance he be tempted to purchase something that he did not intend to buy but merely because he sees it in the store, you place all your accommodation as near the door as possible, so as to keep him from seeing these goods and so to avoid leading him or her into temptation.

Should the potential customer penetrate your first line of defense and actually get a glimpse at your shelves or show cases, he is still protected against a possible impulse to buy. You have seen to it that the goods are in an "artistic" state of arrangement so that the wandering eye may not be caught by an alluring article of luxury. Nor have you been careless enough to mark the prices plainly on those articles which in spite of all care insist in protruding themselves on the unwary customer. The price on the article may show to the observer, that he could afford to buy it and, horror of horrors, may even lead him to do so—and that of course would be against all rules of altruism and philanthropy.

*Personal, or Direct Advertising.*—Some time ago, my boy received a postal card on the morning of his birthday anniversary. It was a picture postal card and had the greetings and the good wishes of a well-known clothing firm. It specifically mentioned the date and also age of the boy. Of course the boy was happy and mother was very much pleased with this attention. Do you think you could get either of them to go to any other store for the boy's furnishings?

Now supposing we find that Mrs. Jones or Smith or Brown is purchasing castile soap and germicides and cotton and gauze, and has a prescription for ergot, etc., it would not require the sagacity of Sherlock Holmes to figure out what is about to happen. And supposing furthermore that by a little judicious inquiry, or by having



someone detailed to watch the daily papers or in many of the numerous means for gathering news, we learn that the expected increase has arrived, and supposing furthermore, we have a neat little inexpensive card, or better still, a personal letter which tells the proud parents how happy we are to know that they are happy. Or supposing we sent a little sample of our pet talcum powder, or some other toilet article of our *own* make, with our compliments to the New Arrival. Do you suppose happy Mamma and proud Father will get real angry at you and come over and slap you on the wrist? If you think so, just try it. I have.

And last but not least: *Service*.—By service I do not mean servility, that has gone out of style with kings and other archaic institutions. I mean the kind and courteous attention which a gentleman may show another gentleman or a lady and only be the more of a gentleman because of such service. Prompt attention to the incoming customer. Courtesy whether a sale is made or not. All the legitimate available information asked for, and given in such a manner that it will create the impression in the would-be or potential customer, that there is truth indeed in the Biblical word: "Happy is he that gives and he that receives."

These are a few thoughts along the lines of legitimate, inexpensive and profitable advertising which I like to have you take home with you. And I have no doubt that most of you can elaborate on them and develop a system of advertising which will be both interesting and remunerative.

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## SIR WILLIAM CROOKES.

BY SAMUEL P. SADTLER, PH.D.,

PHILADELPHIA, PA.

On April fourth last, there died in England one of the most distinguished men in the chemical profession. Sir William Crookes had reached his eighty-seventh year, and during that long term of years he had made his name known in a number of branches of science, which touched upon a great many most interesting and useful discoveries. He was particularly noted by his extremely acute powers of observation, his marvelous experimental skill, and

his powers of philosophical deductions. His researches covered various fields of chemistry and physics, but chiefly those which were within the borderland of these two branches of science. His name was almost equally known, by his long-continued publication and his editorship of the *Chemical News*, one of the best known weekly chemical journals, and the authorship of a number of chemical and technical manuals.

He was one of that class of students who obtained their earliest chemical education at the Royal College of Chemistry, then under Professor Hoffmann, from which institution it will be remembered, came the brilliant work of Perkin, and the discovery of the first of the aniline dyes, together with other valuable work, about the middle of the last century.

Crookes, for a short time, acted as an assistant to Hoffmann and became a lecturer on chemistry in Chester, but after a short teaching experience he returned to London and founded the *Chemical News*, which he edited almost to the end of his long life. It is interesting to note that among the earliest matters which appeared in this journal, were Crookes' reports on Faraday's famous Christmas lectures at the Royal Institution on "The Chemical History of the Candle."

About this period the researches of Bunsen and Kirchhoff on spectrum analysis, leading to the discovery of caesium and rubidium, were made known to the scientific world. Crookes immediately became interested in the use of this new method of analysis and with its aid made his first important contribution to chemical science in the discovery of another new element—thallium. His researches upon the new metal led him into the study of other materials, with the aid of spectrum analysis and he made an extensive study of pure selenium. In connection with the very careful study of these relatively rare metals, Crookes was led to make his weighings on a delicate balance in vacuo. When these weighings were made in this way and in full daylight, irregularities in the action of the balance became evident to the keen observer. He thus found that light objects which were free to move in high vacua could be made to do so by mere exposure to light, and the result was the discovery of the now familiar "Crookes' radiometer," the vanes in which are set in rapid motion when a beam of sunlight is allowed to fall on the apparatus. This study of such "repulsion resulting

from radiation" was pursued by Crookes with extraordinary skill and ingenuity in devising experiments in various directions, and thus he opened up a new and wonderful field for research in molecular physics.

After considerable study of this radiometer the conviction was established that the motion of the vanes in the instrument was probably due to their bombardment by the residual molecules of the high rarefied air in the bulb, being projected from the sides of the same against the movable vanes. Crookes devised many beautiful experiments in this connection and he was thus led on to the study of cathode rays and the bombardment with them of various forms of solid matter which became phosphorescent under their impact. In this way, Crookes developed his theory as to the existence of radiant matter, which he considered a fourth form of matter, showing properties not possessed by matter in solid, liquid or gaseous form.

We have more recently come to speak of emanations in connection with radio-active matter, but it is interesting to note here that Crookes in his earlier researches paved the way for much of our present understanding of radio-active phenomena. One of Crookes' inventions developed after the beginning of the work on radio-activity was the "spintariscopes" in which a screen of natural zinc sulphide is made to scintillate by the alpha particles projected from radium, which furnishes us one of the most beautiful demonstrations, at once visible to the eye, of radio-activity. Crookes made many other very delicate and skillful experimental studies in this same connection of radio-activity, studying the radio-emanation upon a great variety of materials.

In any account of Crookes' career, we must not omit to note many of his speculative addresses and papers, as for instance his interesting paper on the genesis of the elements, delivered as an address to the Chemical Section of the British Association in 1886 at Birmingham. He also became more or less of a spiritualist and wrote a number of papers dealing with these phenomena, which are again exciting the interest of a number of scientific men, perhaps more in England than in this country. One of the most interesting of Crookes' addresses was his address as President of the British Association at Bristol in 1898 in which he discussed the nitrogen problem and called the attention of the scientific world to the rapid exhaustion of the natural nitrogen-containing minerals and the



need of some method for the fixation of atmospheric nitrogen to supply the growing world demand for fertilizer material. There is little doubt but what this address of Crookes', which attracted wide attention at the time, drew the attention of scientific investigators to the question of the synthesis of nitric acid and other nitrogen-containing materials which has culminated in such magnificent results in the various processes of nitrogen fixation, both direct and indirect, which are now being applied in almost every country where the conditions of economical power are such as to make them possible.

Crookes served on many public commissions and lent his powers of observation and analysis to the solution of many technical problems, furnishing a fine illustration of the value of a scientific man to the public welfare, when demands arose for such a study of the public needs and national problems.

Crookes had been a member and president of the several English societies interested in chemistry, including the Royal Society, the English Chemical Society, and the Society of Chemical Industry. He also received the highest honors, including that of knighthood, from his own country.

Crookes illustrated in a very notable degree what might be called a distinguishing character of many English scientific men, namely the ability to do brilliant work in a number of lines, covering a wide field, and including chemistry, physics and technology.

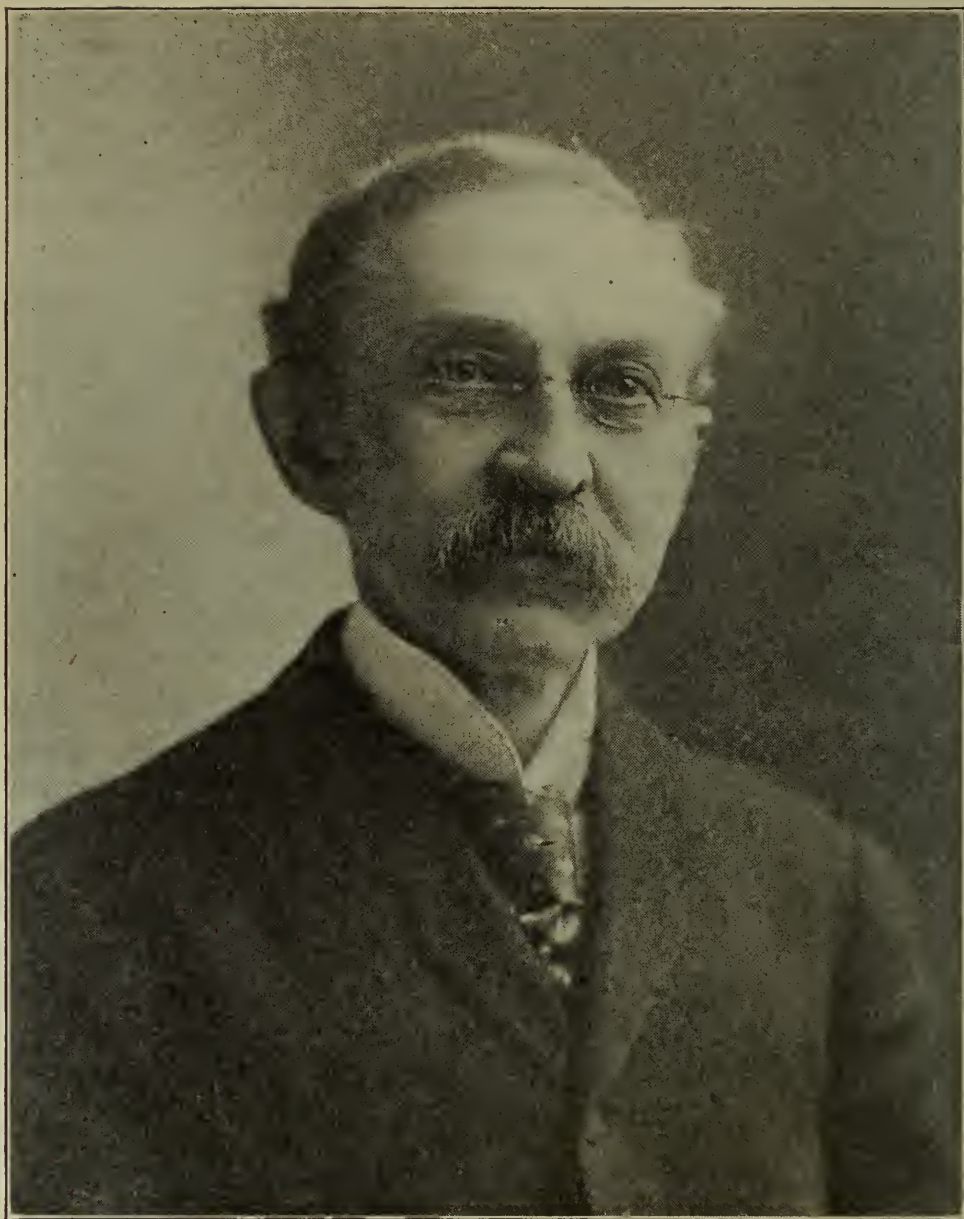
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## JAMES MICHENOR GOOD.

BY HENRY M. WHELPLEY, PH.M.,

ST. LOUIS, MO.

One by one the landmarks in American pharmacy pass away and the succeeding generation fills the places and continues the work. The most recent death attracting general attention is that of Professor James M. Good, who, after a gradual decline in health for a few years and a critical illness of several days, passed to the beyond. His going was as quiet and the funeral as unostentatious as had been the long and useful life of the man. He was cremated and the ashes buried in the same lot with those of Mrs. Good, who pre-



JAMES MICHENOR GOOD,  
Born, January 12, 1842; deceased, May 15, 1919.

ceded him a few years ago. In keeping with his foresight and methodical habits, he sold his store ten days before his death.

Professor Good was not a rapid worker nor a man of quick action or snap judgment. He led a busy, steady and very resolute life. He was recognized wherever he went as a man of integrity and with a well-defined character. While not unchanging nor unchangeable in a broader sense, he remained adamant as far as his purpose and principles in life were concerned. His interest in national affairs and questions immediately vital to the country was constant and much of the time of the past few years was devoted to the reading of current literature dealing with world affairs. He was a staunch Republican in principle, but not dogmatic in politics. Born and raised and married as a Quaker, he continued a Quaker in spirit and principle throughout life. Being quite alone as Quakers, Professor and Mrs. Good early affiliated with the Church of the Unity, finding it an acceptable place for them to worship. Professor Good was for a quarter of a century a director in the church and for many years the treasurer.

The pharmacists of the country at large knew Good best on account of his long and active work in the American Pharmaceutical Association. He joined during the St. Louis meeting in 1871, became third vice-president in 1890 and president in 1895. His work as chairman of the council from 1888 to 1894 caused the officers and other active members to recognize his executive ability and parliamentary efficiency. In 1894, he served as chairman of the Section on Education and Legislation. Pharmaceutical literature received occasional contributions from his pen. They were always along educational, legislative or practical lines. His papers were very much to the point and free from embellishing verbiage. As a speaker, Professor Good held the close attention of conventions and made his points as he went along without eloquence or oratory.

In pharmacopœial affairs, Professor Good dates back to the convention of 1890. He was a member of the Committee on Revision from 1900 to the time of his death. He was also interested in the National Formulary and its propaganda.

Professor Good had an intense conviction of the value of pharmaceutical bodies and practiced his preaching that all druggists should support their local, state and national organizations. He joined the Missouri Pharmaceutical Association in 1880, was treasurer from 1883 to 1887 and president in 1888. He was secretary



of the St. Louis Board of Pharmacy which was created by city ordinance and in operation for a few years previous to the passage of the state law in 1879.

In local drug circles, Professor Good participated as soon as he located in St. Louis, in July, 1868. He filled offices in the successive retail associations that were active at one time or another during his fifty-one years in the city. He was president of the Cinchona Club at the time of his death.

Although known as a retailer, a teacher, a citizen, a husband and a father, it was as professor of theoretical pharmacy in the St. Louis College of Pharmacy that he became familiar to the greatest number of druggists of the Mississippi Valley. He began in the school as vice-president in 1873, being elected to the faculty when Professor Hubert Primm retired in 1875. He gave up teaching in 1916 and became emeritus professor. It was in 1880 that he was elected dean, continuing the work until 1904. Professor Good started life as a farmer boy and he received his early education in the local schools of eastern Pennsylvania. Going to Philadelphia in 1865, he taught for a time in the Friends' School. He attended the Philadelphia College of Pharmacy, completing the junior course in 1867-1868. He often referred to his being a member of private classes under Professor Parrish. His instructions in pharmacy took the pedagogic form. He was quite as particular about having students dot the "i" and cross the "t" as he was in bringing the pupils up to the standard on purely pharmaceutical information.

During the half century in which he was active in the pharmaceutical world, he was always held in high esteem. The Missouri Medical College conferred on him the degree of doctor of medicine. He received from the Philadelphia College of Pharmacy the degree of master of pharmacy at the same time as George M. Beringer, whom he thereafter addressed at "Brother George." He felt particularly dear and near to several men prominent in the pharmaceutical activities, located in different sections of the country. He considered it a privilege to have been intimately acquainted with men along the line from the days of Markoe, Parrish, Maisch, Bedford, Ebert, Hallberg and Remington. He was far from a hero worshiper, but glad to recognize and give full credit to the worth of such men.

It was in Philadelphia in 1865 that James M. Good apprenticed to the firm of B. N. Bethal & Co. He always considered himself a

Philadelphian, although recognizing his obligation to St. Louis, which to him was the city of his adoption. His early experiences in the retail business in the Mound City were very pleasing, bringing him in intimate association with the leading physicians of the day. His first location was at 22d and Clark Avenue, where he remained for twelve years. He then moved to the southeast corner of Jefferson Avenue and Olive Street, where he was until fifteen years ago, when changes in the building necessitated moving and he bought out a competitor on the northwest corner of the same street. The neighborhood had decidedly changed. Many customers and physicians urged him to join them in the western part of the city, but he remained at his old post even though the trade was not of as congenial a character.

The Good Pharmacy always had plenty of clerks. They were given ample vacations and treated in a way that won the universal praise and esteem of all who ever worked in the store. Professor Good believed in the apprenticeship system and was thorough in drilling those who came to him to learn the business.

J. M. Good formed the personal acquaintance of one salesman in each line which he handled and gave them his exclusive business. Other salesmen who called were treated courteously, but found themselves unable to obtain orders. He had his own ideas about conducting business and became quite vexed and even resentful when, a few years ago, I suggested to him that a partner might assume some of the responsibility of the store and relieve him of worry.

A good physique and excellent health were among the assets in life which Professor Good enjoyed. He was plain but neat in dress, reserved but courteous to strangers. He was fond of horses but never ventured to run an automobile. His tenderness of heart for dumb animals is illustrated by an incident which a former clerk relates. A salesman drove up on a cold, stormy day and rushed into the store without blanketing his horse. Professor Good saw the animal shiver and asked the salesman why he did not put on a blanket. The man said that he was in a hurry to get in the store. Professor Good answered, "I will give you time to go out and blanket the horse and you need not come back for an order to-day."

Professor Good was 100 per cent. American long before that expression became commonplace, during the World War. In fact, he was a man who measured up 100 per cent. in all of his ruling

traits of character. Many and interesting are the anecdotes and other pleasing experiences with him which might be recorded if space would permit.

Professor Good is survived by a sister and a married daughter, the latter now Mrs. T. Conzelman, who, as a child and young lady, attended many meetings of the A. Ph. A.

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## A BILL TO IMPROVE THE STATUS OF THE HOSPITAL CORPS OF THE UNITED STATES NAVY.

On June 4, Congressman George P. Darrow, of Philadelphia, introduced a bill designed to effect a commissioned organization of the Navy Hospital Corpsmen which was referred to the Committee on Naval Affairs. During the war the ability of the naval hospital corpsmen was tested in many ways and, in the opinion expressed by many of the naval officials who were in a position to observe the results, they acquitted themselves very well. The navy has for many years been developing a plan for better hospital service and for gradually securing in this service a higher grade of young men whose personnel and attainments would justify advancement to commissioned rank.

Under the provisions of the war measure, providing for the enlarged navy contemplated, a number of the chief pharmacists of experience in this branch of the navy were temporarily commissioned. The purpose of the proposed enactment is to make the ratings then granted permanent and to establish an efficient Hospital Corps as a recognized branch of the Navy Medical Department and under conditions that would induce men of education and ability entering this necessary line of the service.

Pharmacists in civil practice should give this measure their whole-hearted support and endeavor to secure the passage of this bill as an encouragement to those who are endeavoring to serve their country as pharmacists in the navy hospital corps and often under very trying conditions. The pharmaceutical organizations and the pharmaceutical journals will doubtless energetically support the measure, which is reprinted in full as follows. The AMERICAN JOURNAL OF PHARMACY unqualifiedly endorses the bill and hopes for its early consideration and passage.



H. R. 4760.

A BILL.

TO INCREASE THE EFFICIENCY OF THE MEDICAL DEPARTMENT OF THE UNITED STATES NAVY AND TO IMPROVE THE STATUS AND EFFICIENCY OF THE HOSPITAL CORPS OF THE UNITED STATES NAVY.

*Be it enacted by the Senate and House of Representatives of the United States of America in Congress assembled,* That the President of the United States is hereby authorized to appoint and commission, by and with the advice and consent of the Senate, officers in the Hospital Corps of the Navy, in addition to chief pharmacists and pharmacists, at the rate of one for each two thousand of the total authorized number of officers and enlisted men of the Navy and Marine Corps, with ranks of lieutenant commander, lieutenant (junior grade), and ensign, which ranks are hereby established, who shall perform such duties in the Hospital Corps, as part of the Medical Department of the Navy, as may be prescribed by the Secretary of the Navy. Original appointments to fill vacancies shall be made in the rank of ensign, Hospital Corps, United States Navy, by selection from the total number of chief pharmacists and pharmacists, United States Navy, the board of selection for naval medical officers, whenever convened, to constitute a board for this purpose. Chief pharmacists and pharmacists, so selected, shall, prior to promotion be required to successfully pass a physical, mental, moral, and professional examination before medical and professional examining boards appointed by the Secretary of the Navy, and shall have been recommended for appointment by such board. Officers so appointed shall, after serving as ensign, Hospital Corps, United States Navy, for three years, be eligible for promotion to the rank of lieutenant (junior grade), Hospital Corps, United States Navy, and when so promoted shall take rank and precedence with officers of the Naval Medical Corps of the same rank according to the dates of their respective commissions, and such officers shall be eligible for advancement in rank in the same manner and under the same conditions as officers of the Naval Medical Corps with or next after whom they take precedence, and shall receive the same pay and allowances as officers of corresponding rank and length of service in the Naval Medical Corps up to and including the rank of lieutenant commander. Officers of the rank

of ensign, Hospital Corps, United States Navy, shall receive the same pay and allowances as officers of the same rank and length of service in the line of the Navy: *Provided*, That lieutenant commanders, Hospital Corps, United States Navy, shall be eligible for selection by the board of selection of naval medical officers, for advancement in pay and allowances, but not in rank, to and including the pay and allowances of commander and captain, subject to such examinations before advancement as the Secretary of the Navy may prescribe, except that the number of lieutenant commanders with the pay and allowances of captain shall not exceed  $4\frac{1}{2}$  per centum and the number of lieutenant commanders with the pay and allowances of commander shall not exceed 8 per centum of the total authorized number of officers in the Hospital Corps, exclusive of chief pharmacists and pharmacists: *Provided further*, That lieutenant commanders, Hospital Corps, United States Navy, shall be eligible for advancement to the pay and allowances of commander and captain when their total service as officers, exclusive of their service as chief pharmacists and pharmacists, in the Hospital Corps of the Navy is such that if rendered as officers of the Naval Medical Corps it would place them in the list of medical officers with pay and allowances of commander or captain, as the case may be: *And provided further*, That officers of the Hospital Corps of the Navy who shall have gained or lost numbers on the Navy list shall be considered to have gained or lost service accordingly. Ensigns, lieutenants (junior grade), lieutenants and lieutenant commanders, Hospital Corps, United States Navy, shall become eligible for retirement in the same manner and under the same conditions as now prescribed by law for officers of the Naval Medical Corps, except that section 1445, Revised Statutes of the United States, shall not be applicable to these officers and they shall not be entitled to rank above lieutenant commander on the retired list, or to retired pay above that of captain: *And provided further*, That chief pharmacists and pharmacists appointed assistant surgeons (temporary), United States Navy, pursuant to an act of Congress approved May 22, 1917, volume 40, Statutes at Large, page 84, entitled "An act to temporarily increase the commissioned and warrant and enlisted strength of the Navy and Marine Corps, and for other purposes," shall, upon the passage of this act, subject to passing such examinations as the Secretary of the Navy may prescribe,

be immediately eligible for appointment as ensign, lieutenant (junior grade), lieutenant, or lieutenant commander, Hospital Corps, United States Navy, in the ranks held by them as temporary assistant surgeons: *And provided further*, That if any such officer in examination be found by the naval examining board not qualified for appointment in the rank held by him, such board will proceed with the examination and determine the rank, if any, for which such officer is qualified, and shall report its findings and recommendations to the Secretary of the Navy, and if it be found that any officer so examined is not qualified for appointment in the rank for which examined, or in any lower rank, the board shall so report, and if such officer be found not qualified for appointment, or shall refuse to accept appointment in the rank for which qualified and recommended, his temporary commission as assistant surgeon, United States Navy, if still in force, shall be revoked; *And provided further*, That officers so commissioned in the Hospital Corps of the Navy shall retain the precedence with officers of the Naval Medical Corps that they held as temporary assistant surgeons, except that officers found qualified for a lower rank than that held by them in the temporary Navy shall be given a date of precedence as determined by the Secretary of the Navy: *And provided further*, That nothing herein contained shall be construed to legislate out of the service any officer now in the Medical Department of the Navy or to reduce the rank, pay or allowances now authorized by law for any officer of the Navy.

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#### PHARMACY IN THE ITALIAN ARMY.<sup>1</sup>

One of my most interesting experiences, during the five years of war, was the time spent with the Italian Army. I arrived with the British and French troops, sent to the assistance of our Italian comrades, in the black days of November, 1917. The Italians, after a series of magnificent victories and after almost superhuman military engineering feats in the construction of roads and tunnels over inaccessible mountains, had suddenly collapsed, and were in full retreat before the Austro-German forces. The arrival of the British and French troops stemmed the tide of the Austrian advance and the Italian Army made the finest recovery in history.

<sup>1</sup> Reprinted from *The Chemist and Druggist*, June 14, 1919.



The Austrians were held on the Piave, and, on the mountain passes, their renewed attack in the following June was repulsed with the heaviest loss, and they were hurled back into their own territory in October, 1918.

As in the case of the French *Service de Santé* in order properly to appreciate the position held by pharmacy in the army of our Italian Allies, it is necessary briefly to sketch the organization of the Italian Medical Service. Italy as a unified kingdom is of so recent a date that its Medical Service might be thought to have no history; but this is hardly the case, for so far back as 1833 we find an organized service in what was then the kingdom of Sardinia, with one pharmacist to about every ten medical officers. It is noteworthy, also, that the organization of the Army Medical Service, in the form of autonomous medical units, was adopted earlier in Italy than in any other continental country.

The Army Medical Inspectorate at the Italian War Office consists of an Inspector-in-Chief, assisted by five inspectors, of whom one is a pharmacist officer designated "Inspector of Pharmacy and Chemical Services."

GRADES OF THE ITALIAN MEDICAL SERVICE.—The medical officers of the Italian Army and Italian Red Cross—to which I will refer subsequently—have ordinary military titles followed by the word "Medico." Pharmacist officers do not, however, hold ordinary military titles. They are graded as follows:

*Chemico farmacista ispettore*, ranking as colonel.

*Chemico farmacista direttore*, ranking as lieutenant-colonel.

*Farmacista Capo di 1a Classe*, ranking as major.

*Farmacista Capo di 2a Classe*, ranking as captain.

*Farmacista di 1a Classe*, ranking as captain also, but drawing less pay than the *Farmacista Capo di 2a Classe*.

*Farmacista di 2a Classe*, ranking as lieutenant.

*Farmacista di complemento di 3a Classe*, ranking as second lieutenant.

As in the case of the Australian Commonwealth Forces, there are no distinctions in the emoluments of different branches of the Italian Army. All officers, whether combatant, medical or pharmaceutical, draw the pay of the rank to which they belong. Medical officers draw a small additional special allowance, but the privilege is not shared by their pharmaceutical colleagues. Pharmacist and medical officers wear the same field gray uniform as other officers,

the color of which is now fairly familiar in the streets of London. The different regiments, administrative and other services, are distinguished by different colored, gorget patches. Medical officers wear dull cherry-colored, and pharmacists black patches, on their collars. All grades of the Italian Army, from private to general officer, wear the five-pointed star of United Italy on the collar-patch. Medical officers and pharmacist officers of the Italian Red Cross have the same badge as military ranks, but with a small red cross in the center of the star. The cap badge of all grades of the medical service is a five-pointed star enclosing a minute red cross and surmounted by the royal crown.

THE MEDICAL SERVICE IN THE FIELD.—The medical service with an army in the field is divisible into three groups: (1) Divisional, (2) Corps, (3) Army.

1. *Divisional*.—As in the French Army each regiment—which, it will be remembered, corresponds with a British brigade—has its own regimental medical staff, but in the Italian Army there is no pharmacist officer in charge of the regiment, as with the French. Each division has one *Sezione di Sanità*, which is responsible for the evacuation of wounded from the regimental aid posts back to the field hospital. There is no pharmacist with this formation, which corresponds with the *Groupe des Brancardiers Divisionnaire*, or Divisional Bearer Company of the French rather than with our field ambulances.

2. *Corps*.—The Italian Army is organized on a corps basis, and therefore the *Direttore di Sanità*, who corresponds with the Deputy Director of Medical Services in our army, has much more power and authority than has his British colleague. The Italian officer corresponding with our Divisional A.D.M.S. is only a major, and has comparatively little administrative work or responsibility. In our army the Divisional A.D.M.S. and Corps D.D.M.S. are both full colonels, and, whereas the former has three units under his immediate command, the latter has no medical formations under his direct control.

Each Italian corps has attached to it from twenty to thirty *Ospedali di Campo*, with an aggregate of two thousand beds. *Ospedali di Campo* are field hospitals, and provide accommodation for 50, 100 or 200 patients.

It is with the hundred-bedded hospital that we first find the pharmacist officer. The personnel of these units is: Three medical

officers, one pharmacist, two quartermasters, thirty-eight rank and file.

The Director of Medical Services of the Italian Corps takes over all wounded and sick at the *Posto Smistamento*, or divisional dressing-stations of his divisions, and distributes the cases to these field hospitals. The *Ospedal di Campo* therefore act as casualty clearing stations for the divisions. They are mobile, but may be immobilized for special work, such as infectious hospitals. On the plains they are located in palaces, villas, schools or theaters, but in the mountains special wooden huts are erected for them by the engineers. All are furnished with collapsible iron beds, sheets and blankets. In all these hospitals special attention is given to the *Farmacia*, which I found invariably well stocked and equipped.

DISINFECTION AND WATER-SUPERVISION UNIT.—With each corps is a special unit, corresponding, more or less, with our sanitary sections, but equivalent in strength to four of our sanitary formations. There is a medical officer in charge, a pharmacist officer, two engineer officers, and one hundred other ranks.

The pharmacist officer is the consulting chemist and analyst of the section, and, by virtue of his position, the adviser on all chemical matters to the Director of Medical Services of the Army Corps. In an Italian Army Corps he, therefore, holds a responsible and honorable position which has no analogue in the British service.

3. *Army*.—An Italian Army consists of a group of three or more army corps. The medical services of each Army is under the direction of a *Direttore di Sanita d'Armata*, who is a *Maggiore-Generale Medico*, or surgeon-general. He has on his staff eight medical and four pharmacist officers. The Chief Pharmacist of the Army is responsible to the director for the care of all drugs, dressings, medical and surgical appliances in the Army area. He carries out, on behalf of his chief, inspections of military pharmacies, chemical and scientific laboratories and advanced depots of medical stores.

CARE OF MEDICAL AND SURGICAL STORES.—As in the French and other Continental armies, the care of medical and surgical stores is entirely in the hands of pharmacists. In our Army the care of advanced and base depots of medical stores has been in the hands of Royal Army Medical Corps quartermasters throughout the greater part of the European War. In the South African and all previous wars, these depots have been commanded and administered by medical officers.



The chief source of drugs, dressings, and medical and surgical appliances for the Italian Army is the *Farmacia Centrale Militare* at Turin, which is under the command of the *Chemico Farmacista Direttore*, who has a large staff of pharmacist officers and subordinates.

The Central Military Pharmacy is organized in six sections, each under the command of a pharmacist officer. These sections are as follows:

- (1) Analytical Laboratory.
- (2) Pharmaceutical Laboratory.
- (3) Quinine Factory.
- (4) Bacteriological Laboratory.
- (5) Surgical Dressing Mill.
- (6) Packing, Receiving and Distributing Stores.

The "Pharmacy" is, in short, a wholesale drug-store of the largest and most up-to-date kind. The machinery for making tablets is of the most modern description, and the preparation of hypodermic solutions is a special feature of the establishment. All hypodermic solutions are packed in small phials containing one dose.

The quinine factory was, before the war, the most important part of the pharmacy. It supplied not only the Army, but many civil institutions in Italy and elsewhere. Malaria is common in parts of the kingdom, and, as in India, the state, aided by the *Croce Rossa Italiana*, makes special arrangements for the sale and gratuitous distribution of quinine to the public.

The Central Pharmacy was able to turn out 300,000 five-grain tablets of quinine daily, and, in addition to supplying its own needs before the war, the Italian Government was able to export quinine to Turkey, Greece, the Balkan States, and many other countries. The Central Pharmacy distributes supplies to regional and army pharmacies, on which all military hospitals and formations in the region or army indent for their requirements.

RECRUITMENT OF PHARMACIST OFFICERS.—The Italian Army Medical School is at Florence. It is an institution exactly similar to our Royal Army Medical College. Like our college, it differs from the French and other continental military medical schools in the fact that it is attended only by graduates in medicine of the universities who are candidates for commissions in the regular army or for the rank of surgeon-lieutenant in the reserve. Pharmacists do not pass through this school. Students of pharmacy enter com-

panies of the Army Medical Service, and on passing an examination become pharmacist cadets with the rank of corporal or sergeant. On graduation in their universities they go through a special course of instruction, and may then present themselves for examination for advancement to the rank of *Farmacista di Complemento di 3a Classe* (pharmacist officer of the reserve), with the rank of second-lieutenant. On attaining this rank the pharmacist officer may serve the remainder of his period of liability to military service in the reserve, or may enter for a competitive examination for a commission in the standing army. If successful he is gazetted a *Farmacista di 2a Classe*, with the rank and pay of lieutenant.

From this grade he is promoted by seniority or selection. In peace there are, as in the case of the British service, medical officers' examination for each step in rank, but these are, of course, abolished in war time.

In addition to the pharmacist officers and cadets there is a considerable personnel employed on pharmaceutical duties. These are the medical assistants or *aiutanti di sanita*, who are recruits from among the students of medicine, science, and pharmacy of the universities. Young priests are also liable for service as medical assistants. These medical assistants have the rank of corporal and lance-corporal, forming a section in each company of the Army Medical Service apart from the nursing, clerical and stretcher-bearer sections.

In addition to the pharmacists of the Regular Army the Italian Red Cross, or *Croce Rossa Italiana*, employs a very large number of graduates in pharmacy of the universities.

The Red Cross enjoys a very honored and important position in Italy, and its personnel is to some extent exempted from ordinary military service.

It has long anticipated the present scheme for utilizing the Red Cross in peace time, and had, for instance, a well-organized anti-malarial service long before the war. Quinine was distributed at the expense of the government and of the society by trained pharmacists.

It will be seen by readers of the article on "Pharmacy in the French Army,"<sup>2</sup> that the profession of pharmacy holds a high and honored place in the French Army, but that, although Italy is almost as democratic a country as France, the pharmacist official is

<sup>2</sup> *Chemist and Druggist*, June 7, p. 50.

on a somewhat lower plane than with the army of the Great Republic, where the *pharmacien* and *médecin* are, in every sense of the term, "Brothers in Arms."

M.D., L. P. S. I.

## THE PURITY OF COMMERCIAL ASPIRIN AND ASPIRIN TABLETS.<sup>1</sup>

BY A. J. JONES.

In the earlier stages of the manufacture in this country of aspirin, it was almost impossible to maintain a supply of the product of the recognized standard, such a condition of affairs being what is expected when the inexperience and difficulties attending a new manufacture are taken into account. Some samples were very good, others graded down to products that could not be passed at all, whilst frequently the purchaser's only option was to buy the least faulty samples on offer at the time. Many were not of the standard of the British Pharmacopœia, and the opinion was even expressed that the official standard was commercially impossible. The characters and tests of the British Pharmacopœia do not admit the question of grade, nor are they sufficient to offer any help when that matter becomes involved. In such cases a more detailed examination is necessary, and the present paper is a note of results and observations made in this direction. The samples are of moderately recent date, and, since a much better stage of stability in the manufacture has now been reached, these are fairly representative of the current market.

### METHODS OF TESTING.

The tests used in the case of the samples of aspirin in question consist of determinations of acid, ester, and bromine values, together with free salicylic acid, and melting-point. For the better comparison the results are expressed in Cc. *N*/5 per 1 gram of substance, the bromine value being reduced to terms of a monobasic reaction: that is to say, one atom of bromine per molecule. Under these conditions it is clear that with true acetylsalicylic acid the

<sup>1</sup> Reprinted from *The Chemist and Druggist*, April 26, 1919.



three sets of figures should be identical. The details of the pouring the caustic into the acid.

*The bromate solution* consists of potassium bromate ( $\text{KBrO}_3$ ) 5 grams and potassium bromide ( $\text{KBr}$ ) 20 grams, water 1,000 Cc.

*The N/10 thiosulphate* is standardized against the iodine liberated from potassium iodate ( $\text{KIO}_3$ ) and potassium iodide ( $\text{KI}$ ) by a given amount of the *N/5* acid used above, this precaution being taken so that strict comparison is possible, all titrations being really in terms of one standard solution—the original *N/5* acid.

soda free from carbonate, setting this with phenolphthalein and run-

#### DETERMINING THE ACID AND ESTER VALUE.

One gram of the sample is accurately weighed and rinsed into a flask with about 15 Cc. of absolute alcohol (B.P.); solution being complete, phenolphthalein is added, and the titration made with the *N/5* soda. Fifty Cc. of the same soda solution is now added from a pipette, and another 50 Cc. taken, draining the pipette in exactly the same manner, for a blank. Reflex tubes are fitted, the flasks set in a water-bath for about twenty-five minutes, then cooled and titrated back with the acid; the difference between the blank and test titers being the number of Cc. *N/5* equivalent to the ester, and cedure adopted in the tests are as follows:

*Standard N/5 acid* is prepared and a similar solution of caustic should (theoretically) be identical with the acid titration.

As it is quite possible for slight hydrolysis to occur while determining the acidity, comparative tests were made by estimating the difference in the amount of free salicylic acid before and after titration. Standard acid, equivalent to the number of Cc. of alkali used in the test, was returned to the titrated liquid before the comparison was made by the iron test. Half a gram of aspirin was used, and it was found that 0.1 to 0.5 milligram were the extreme limits due to titration, with a fair average of 0.3 milligram—or, say, 0.02 Cc. *N/5*—for one gram. Since this is accompanied by its equivalent of acetic acid an adjustment is required in the relative acid and ester values. One should, therefore, deduct 0.02 Cc. from the experimental acid figure and add it to that of the ester.

#### THE BROMINE VALUE.

Accurately weigh 0.5 gram of the acetylsalicylic acid, wash into a flask, add 15 Cc. *N/5* soda, and set in a water-bath as described

RESULTS OF THE EXAMINATION OF SAMPLES OF ACETYSALICYLIC ACID.

Origin.	Acid Value.	Ester Value.	Total.	Bromine Value.	Salicylic Acid, % ex Br. Value.	Free Salicylic Acid.		Melting Point.	Behavior with Iron.	In Soda Solution.	
						%.	Eqvlt. c.c. N/5 per Gram.			Color.	Odor.
Theory.....	27.769	27.768	55.537	27.769	76.66	0	0	133-135° C. and 137° C.	—	—	—
GROUP I											
1. N. England .....	27.74	27.70	55.44	27.78	76.68	0.05	0.02	135-136	clear	{ pale straw	faintest trace of pyridine
2. S. England .....	27.60	27.59	55.19	27.67	76.38	0.3	0.11	132	clear	yellow	not at all good
3. S. England .....	27.70	27.58	55.28	27.82	76.78	0.075	0.03	135-136	clear	{ pale straw	none
4. Japan .....	27.83	27.43	55.26	27.69	76.42	0.113	0.04	134	clear	{ full yellow	distinct smell of acetic ether
5. N. England .....	27.78	27.43	55.21	27.78	76.68	0.20	0.07	—	clear	full yellow	very objectionable
6. } S. England, same make.	{ 27.68	{ 27.43	{ 55.11	{ 27.70	{ 76.46	{ 0.15	{ 0.05	{ 132-134	{ clear	{ pale straw	{ distinct traces of acetic ether
7. }	{ 27.60	{ 27.42	{ 55.02	{ 27.67	{ 76.38	{ 0.175	{ 0.06	{ 132-134	{ clear	{ pale straw	{ distinct traces of acetic ether
8. London broker .....	27.58	27.33	54.91	27.73	76.54	0.075	0.03	135	faint opalesc.	—	—
9. London broker .....	27.78	27.22	55.0	27.68	76.40	—	—	—	—	—	—
10. Unknown .....	27.96	27.23	55.19	27.66	76.34	0.125	0.045	134	clear	buff	slight odor
GROUP II											
11. } American, same shipper	{ 27.20	28.02	55.22	27.89	76.98	0.05	0.02	132	very turbid	very pale straw	faint pyridine and salol
12. }	{ 27.25	28.02	55.27	27.89	76.98	0.05	0.02	132	slight opalesc	{ pale straw	{ trace, aniline-like, with suggestion of salol
13. } Manufacture ceased ...	{ 27.24	27.92	55.16	27.89	76.98	0.125	0.045	134-135	clear	{ pale straw	{ strong aniline-like
14. }	{ 27.48	27.73	55.21	27.64	76.30	0.10	0.036	134-135	very turbid	straw	
15. London Wholesale House	27.38	27.68	55.06	27.83	76.82	0.10	0.036	131			

\* Free salicylic absent by B.P. test.

above. After the twenty-five minutes this solution is cooled to room temperature, diluted and transferred to a 250-Cc. flask, and carefully adjusted to the volume and well shaken. One should be sure either that the instruments are exact or else take the precaution of graduating the flask by ten deliveries, each made in exactly the same manner, from the 25-Cc. pipette about to be used. Twenty-five Cc. is withdrawn by a pipette and delivered into an accurately stoppered 16-oz. shop round; add 25 Cc. of the bromate solution, also very accurately delivered, and then 250 Cc. of water. Fifteen Cc. of hydrochloric acid (B.P.) is added, and the bottle stoppered. A blank is prepared in precisely the same manner, and both are set aside for twenty minutes with occasional shaking. Fifteen Cc. of 10-per-cent. sodium iodide solution is then run in with all necessary precautions, the solution well shaken for a few minutes and then titrated with  $N/10$  thiosulphate, using a solution of soluble starch as indicator. Duplicate tests agree to within 0.05 of a Cc.

To check both solutions and the manipulation comparison was made with two samples of specially prepared salicylic acid. In the test in question this showed 99.9 and 100 per cent. of the acid taken. From the difference between the blank and the test, the number of Cc.  $N/5$  taken by one gram of the aspirin is calculated, dividing this by six—since six atoms of iodine thus shown are equivalent to one molecule of salicylic acid—there is obtained a number of Cc. which should (theoretically) exactly agree with the acid and ester figures.

#### DETERMINING FREE SALICYLIC ACID.

Dissolve one gram of salicylic acid in about 60 Cc. of alcohol, and then adjust to 100 Cc. with water; 10 Cc. of this liquid is diluted to 1,000 Cc., making 1 Cc. equal to  $1/10$  milligram of salicylic acid. Prepare also a 1-per-cent. aqueous solution of iron alum.

For the test, dissolve 0.6 gram of the aspirin in a measuring cylinder with 9 Cc. of alcohol, dilute with water to 90 Cc., and well mix. Take two precisely similar Nessler glasses. Into one pour 60 Cc. of the solution, into the other 30 Cc., together with 3 Cc. of alcohol, and adjust to the volume of the first; this gives a difference of 200 milligrams of aspirin in a mixture of equal parts of alcohol and water. One Cc. of the iron solution is added from a pipette to each, and the color matched by adding the standard salicylic-acid solution from a burette. Supposing 4 Cc. to be required, we then



have 200 milligrams aspirin = 0.4 milligram salicylic acid, or 0.2 per cent. The limit that admits of satisfactory matching is about 0.5 milligram. It has been found necessary to adopt this method because both aspirin and alcohol have an effect on the iron coloration.

The B.P. test, if used with a little discretion in the interpretation of "violet color," is good enough for detecting inferior samples, but in those cases where one hesitates as to whether a sample can be passed, it is sometimes a trifle misleading. The various factors effecting solubility, such as crystalline condition and surface effects, come into play, and where but slight traces are present, a comparison formed on the B.P. test may be reversed on complete solution, as in the test described. It is preferable to adopt the latter test and work to a definite limit.

Another modification of the test is described in the British Pharmaceutical Codex, the Belgian Pharmacopœia, and elsewhere—namely, that 0.1 gram of aspirin when dissolved in 5 Cc. of alcohol and 20 Cc. of water added should give no violet color with ferric chloride. It should be pointed out that in this strength of alcohol the coloration is strongly depressed, and further so by employing ferric chloride in preference to iron alum. It has been found that with this test, and using one drop of 5-per-cent. ferric-chloride solution, a sample containing 0.15 per cent. of free salicylic acid gives only a brownish yellow, with 0.2 per cent. a shade of pink to which serious exception cannot be taken, and with 0.3 per cent. a very distinct salicylic reaction. This test is a good guide for sorting-out purposes and in routine work, but it is not suitable for precise work. Increase in the iron still further depresses the coloration.

#### DEDUCTIONS.

The first thing noticeable is, that there are two distinct varieties of commercial aspirin: one, where the acid is either equal to or exceeds the ester; the other, in which the ester is in distinct excess of the acid as well as being in excess of theory in some cases; while in both groups the saponification value is consistent throughout, and always less than theoretical.

*Acid and Ester Value.*—On examining the figures for samples 1 to 10, it will be seen that if the determination by iron be assumed to measure the dissociated salicylic and acetic acids, in sample 1 the acid exactly agrees with the ester (27.72 and 27.72), and also very

nearly so in the case of sample 3 (27.67 and 27.61), as required by theory, whilst sample 2 is placed in the other group. But in the remaining samples, for a constant value in the ester, the acid varies in the ratio of from 100:100.7 to 100:102.7, and the presumed dissociation does not account for this difference in any degree. It, therefore, appears that there is a certain acidity either in the preparation or developed in solution of many samples, which is neither due to free salicylic acid alone nor to dissociated acetylsalicylic acid.

*Bromine Value.*—In considering the bromine value in its relation to the acid and ester, in the case of the first group, it is seen to approximate the acid value rather than the ester. This is what one would expect, since it is the salicylic group in the molecule that is responsible for both figures. It might further be supposed that any dissociation would be reflected in the acid value exceeding the bromine, the difference being due to dissociated acetic acid and equal to the free salicylic found by the iron test in terms of  $N/5$  soda per 1 gram. If the salicylic acid found occurred as such, and not as a product of dissociation, both acid and bromine value should agree, but on looking into the figures this is seen not to be the case. In eleven out of the fifteen examples the bromine is in excess of the acid, in Group I slightly, in Group II very markedly, and at the same time noticeably agreeing with the ester value.

With regard to these two points, after reviewing the figures and making allowances for the probable dissociation, it would appear that the excess of bromine in the first set of examples can best be explained by assuming salicyl-salicylic acid being present in minute quantities. In the second series one might expect acetyl-salicyl-salicylic acid to be in the main the contaminating substance, as with this substance there are two salicylic groups in the molecule and the ester value is also double the acid value, hence to the extent of its presence in aspirin both ester and bromine value would rise in agreement. Sample 15 is suggestive of both salicyl-salicylic acid and acetyl-salicyl-salicylic acid being present.

In this connection it has been observed that on taking about a gram of the aspirin, fifteen to twenty drops of methyl alcohol, about 8 Cc. of water and adding some crystals of sodium carbonate, warming to effect solution and then boiling for about half a minute, both during the operation and on allowing to cool a strong odor of methyl salicylate is developed in samples of the second group. In those represented by 2, 6 and 10 there is no trace of the wintergreen

odor, while others where the bromine value is high give a slight suggestion.

In the three exceptions (4, 9, 10), which might fall in with the above statement regarding the acid exceeding the bromine value, the excess acid is considerably greater than that due to dissociation, as indicated by the iron test, thus confirming from another point of view what has been said above regarding the occurrence of an acidity not due to acetyl-salicylic acid. This "excess" acidity is not open to any ready or easily demonstrable explanation, but the presence of such a body as salicyl-acetic acid,  $\text{C}_6\text{H}_4 \cdot \overset{\text{O}}{\overset{|}{\text{C}}} \cdot \text{COOH} \quad \text{CH}_2 \cdot \text{COOH}$ , in which there are two carboxyl to but one salicylic group, is very suggestive. With a chemical like aspirin, where a number of secondary products are possible, quite apart from real extraneous impurities, in the absence of specific reactions it is largely a matter of conjecture what the precise substances are that cause the variations in the analytical figures with different samples. That there are traces of other impurities present in some samples is certain, the peculiar odors in the crystals or powder frequently developed by treating with solvents and with alkali, and the different intensity in color of the caustic and carbonate of soda solution all show this. On treating with soda faint odors have been observed suggestive of salol, acetoacetic ester, pyridine, and anilin, and in some cases very strong and objectionable odors difficult to describe.

#### SUGGESTED STANDARD.

The question now remains as to what analytical figures may be considered characteristic of the best grades on the market, and the following is suggested:

Where the acid value is greater than the ester value, that the difference should not exceed 0.3 Cc. *N*/5 soda per gram and the bromine figure should not exceed the acid value by more than 0.15 Cc. in similar terms. Where the ester exceeds the acid, the excess should not be more than 0.3 Cc. *N*/5 soda per gram, and in this case the bromine figure should not exceed the ester value.

For free salicylic acid the limit should be not more than 0.15 per cent., and no turbidity should occur in the iron test.

A good sample should also be given only a very pale straw color when dissolved in 10 or 20 per cent. soda, and there should be practically no odor either in the dry state, in soda solution, or when damped with spirit and water.



The melting point should not be lower than the present official standard. An experience of a very large number of samples shows that the best samples melt at approximately  $136^{\circ}$ . Such specimens have a decisive melting point, varying within a degree in consecutive determinations, and there is a sense of stability which is lacking with the lower figures. Samples which have given subsequent trouble in practical experience have almost invariably been those melting below  $133^{\circ}$  C.

It is sometimes urged that since one of the main objects in the use of acetylsalicylic acid is to provide salicylic acid in an esterified form, from which it is liberated under certain conditions by gradual hydrolysis, the occurrence in aspirin of small amounts of compounds such as salicyl-salicylic acid, which is itself used in medicine, is not a matter of real importance. What may be said for or against this from a pharmacological standpoint, or to what extent such contamination might be allowed in the drug, cannot be entered into here, but if this were agreed to then a test limiting values would be essential unless it is found—and there is a good deal to be said for this—that the present official tests with a definite limit for the free salicylic acid are such as will ensure a product of a sufficient degree of purity for all medicinal purposes, while not demanding refinements the attainment of which would throw an undue burden on the manufacturer without any practical or commensurate advantage to the patient.

#### ASPIRIN TABLETS.

There seems to be an inclination in some directions to look upon tablets as mysterious composts in which very questionable ingredients may be safely hidden, and one finds a good many disappointments in examining these products. In the case of aspirin tablets excessive free acid, very high ester and excessive excipient balanced by deficient aspirin are the chief faults. On examining a series of what may be called "standard" makes all were found to be excellent products in very close agreement, but none was of that superlative quality in relation to any other as one might expect.

Disintegration is a property occasionally lost sight of, and one brand of "chemist's own label" variety, after digesting in water for two days, required firm pressure with a glass rod to break it up. The desideratum is that the tablet should be of good appearance, clean cut and pressed, able to withstand carriage—whether in bulk

or in the tablet-bottle in the waistcoat pocket—yet capable of immediate disintegration in water. In the “standard” series mentioned above all the samples were very satisfactory in this respect. On dropping the tablets into water and allowing them to remain for half a minute without agitation some “effloresced” into a powder, others swelled and parted, and all save one became powder on swirling the test-glass; the exception remained partially powdered, about half the tablet retaining its form, yet being quite soft and dissolving within a minute or two. In this connection it is interesting to note what must indicate variability in machining, which must occur, for on taking six or eight tablets, as was done with one brand, about half of them disintegrated within ten seconds, the remainder taking the full half-minute.

#### ANALYTICAL PRECAUTIONS.

In the examination of tablets certain precautions are necessary on account of the excipient, which, apart from the usual starch, talc and adhesives, sometimes includes small quantities of a wax or fatty substance. Stearic acid has been noted in one or two cases, and if this and substances such as Japan wax are employed it is clear that for very precise work analytical procedure must be modified to meet them. A determination of the free salicylic acid by iron and the total by bromine is perhaps the most satisfactory means of evaluation. In the latter test it is best to extract the tablet with alcohol and filter; add alkali and distil off the alcohol during saponification, then follow the method indicated in the case of aspirin.

For the free salicylic acid, crushing the tablet and applying the B.P. test is not of much value where fatty excipients have been used since, while really containing quite the ordinary traces, the barest evidence is given in the water test. For the estimation it is best to take one, two, or three tablets, grind up in a mortar with 9 Cc. of alcohol and a little kaolin, adding 70 Cc. of water, and drawing through a Gooch filter, then washing with another 20 Cc. of water, the volume being adjusted finally to 90 Cc. and the determination completed as before. Since the difference is one third, it is useful to remember that by multiplying the number of Cc. of standard solution used to effect the match by 0.3 (since 1 Cc. = 1/10 Mgm.) one gets the milligrams of free acid in the tablets taken. For example: two tablets were treated as described, and required 3 Cc. of

the standard for matching; therefore the two tablets = 0.9 Mgm. of free salicylic acid and consequently one tablet (5 grs. or 324 Mgm.) = 0.45 Mgm., or 0.14 per cent. on the presumed aspirin content. In bad cases it may be necessary to make a dilution of one tablet and take an aliquot part of that, say, a fifth or even a tenth.

The following quantities have been found: (a) 0.12 per cent., (b) 0.16 per cent., (c) 1.85 per cent., (d) 0.14 per cent., (e) 0.185 per cent., (f) 0.06 per cent. Samples (a) to (d) are well-known brands of which (c) lays claim to a very high excellence in common with the others; (e) is a "chemist's own label" variety; and (f) occurs in trade without advertisement. Aspirin from the same source as (e) is shown as (2) in the acetylsalicylic acid table on page —. As to the limit of free acid allowable, 0.2 per cent. would cover all reasonable requirements and permit a small margin for deterioration due to the manipulation required in preparing the tablet mass.

The following table gives the analytical figures for five samples selected from different sources: The "values" are Cc. N/5 per 1 gram of the powdered-tablet mass just as in the case of the acid itself, the assay being on the alcoholic extract.

No.	Weight, Grains.	Acid Value.	Ester Value.	Bromine Value.	Free Salicylic Acid, Per Cent.	Aspirin.		Ash, Per Cent.
						Per Cent.	Per Tablet, Grains.	
1	5.60	23.73	23.44	23.91	0.12	86.08	4.82	None
2	5.66	24.62	24.48	—	0.12	88.15	4.98	2.25
3	5.50	25.25	25.17	25.10	Mere trace	90.36	4.97	4.54
4	5.46	21.63	22.98	21.78	Full react.	78.41	4.28	7.20
5	5.17	18.48	20.03	19.59	—	72.0 (approx.)	3.73 (approx.)	3.10

Number (1) is a semi-proprietary, (2) is from a wholesale house, and (3) from a firm of tablet-makers. Numbers (4) and (5) are examples of very inferior products, the last-named being obviously fraudulent.

It should be pointed out that the difficulty with aspirin is one of theory and practice. Acetylsalicylic acid is a definite chemical substance, but in the process of manufacture the difference of *technique* employed, together with the possibilities for secondary reactions, results in the production of an aspirin that departs fractionally from theory. If a manufacturer is producing a chemical which does



so depart, yet is commercially acceptable and medicinally satisfactory, he is hardly likely to modify his output. One has, therefore, to be prepared to meet variation in commercial samples, hence the suggestion earlier in this article. Users of aspirin must, however, exercise care in regard to the development of odor. Sellers will not always recognize the complaint of buyers in this respect, but it is very important. Odor sometimes develops to a remarkable and inexplicable extent in use, and on keeping, which no amount of reference to figures will negative. It is wise to put aside all samples that are the least suspicious in this regard.

It is hoped that the subject of aspirin standards may be of interest to others, and that some further expression of experience and views may be forthcoming.

This note is the result of work carried out in the analytical laboratories of Evans Sons Lescher & Webb, Ltd., at Liverpool.

## THE CHEMICAL ASSAY OF FOXGLOVE.<sup>1</sup>

BY TSCHIRCH AND WOLTER.

Up to the present no reliable chemical assay of foxglove leaves has been devised, and the biochemical method has been more and more generally adopted. The chief constituents of the leaves are digitoxin, digitonin and digitaleins. Digitoxin, the separation of which has hitherto been made the basis of a chemical method of assay, is not a definite substance, but a mixture to which the name of pseudodigitoxin may be applied. Digitalin is a cardiac poison. Digitonin belongs to the saponin group. Digitalein is a group designation for the water-soluble glucosides, one of which (gitalin) produces the specific action of foxglove. The authors tested all the chemical methods of assay that have been proposed by determining the physiological activity of the substance isolated and weighed, and comparing it with the physiological activity of the leaves. They found in agreement with Ziegenbein and with Jermstadt, that the digitoxin content was not in proportion to the physiological activity of the leaves. Keller's process for the determination of digitoxin was carried through and the solutions tested at each step to ascertain where any loss might occur; it was found that five shakings

<sup>1</sup> *Schweiz. Apoth. Zeit.*, Vol. 56, p. 469. Reprinted from *The Pharm. Jour. and Pharm.*, April 12, 1919.

with chloroform were not sufficient to remove all the physiologically active substances; for this eight shakings were necessary. The physiological activity of the digitoxin obtained was, however, not proportionate to that of the aqueous solution before its removal, and the authors conclude from this and other experiments that the original solution contains the active and inactive substances in some form of combination which is broken up by the shaking with chloroform. By means of color reactions it was shown that various menstrua did not effect any separation of the glucosides contained in the leaves that might have been expected from their varying solubility when isolated; they appear, therefore, to influence one another's solubility. Leaves were then extracted with various solvents to determine which exhausts them best. Ether and carbon tetrachloride extract no active substances; chloroform, acetic ether, and benzene exhaust them partially; absolute alcohol, acetone, and amyl alcohol exhaust them completely, but the high temperature necessary for the evaporation of the amyl alcohol solution appears to produce partial decomposition. An objection to the use of acetone as also of alcohol is its miscibility with water; this, however, can be overcome by using a saline solution instead of water. Acetone is preferable to absolute alcohol, as the solution obtained is colorless. The authors finally propose the following method for the chemical assay of foxglove leaves: The leaves are first exhausted with ether, by which chlorophyll, fat and resin are removed. They are then treated according to Keller's method, but after precipitating with lead the glucosides are shaken out with acetone, the acetone solution being made to separate by adding sodium chloride. In this way a mixture of all the active constituents of the leaves is obtained, for which the authors propose the name of *pandigiton*. The physiological activity of the *pandigiton* obtained is, however, less than that of the corresponding quantity of the solution before its removal, although the solution left after its removal is quite inactive. Two explanations of this are possible, viz., either the separation has involved some change or the inactive substances in the liquid exert some favorable influence. Moreover, the weight of *pandigiton* obtained is not proportionate to the physiological activity of the leaves. Nevertheless, the authors claim that the acetone method is a chemical method of assay inasmuch as by it all the active constituents, and not the digitoxin alone, are separated and weighed.

## LIPOVACCINES.<sup>1</sup>

Prophylactic inoculation of great masses of people against infectious diseases, such as typhoid, cholera, dysentery, plague and possibly pneumonia, has for years been an ideal in the minds of many sanitarians, especially those who have been in contact with the populous but disease-ridden oriental countries where even simple methods of sanitation have encountered opposition. Inoculation itself, however, has met so many practical difficulties that it has remained largely an unattainable ideal. With the vaccines heretofore used, a relatively severe local and general reaction followed the inoculation; and while the health officer, by means of a variety of expedients, might send home his first dose of vaccine, it was quite another matter to induce the subjects to come back for more. Nor has this been true in dealing with unintelligent communities only.

Ferran, so far back as 1885, inoculated thousands against cholera in Spain; the work of Haffkine with plague in India is well known; Shiga inoculated against dysentery in Japan, and the more recent work of Lister in South Africa against pneumonia also seems successful. The most pronounced results have been obtained with typhoid-paratyphoid vaccines. The severity of the reactions, however, has been sufficient to make mass application unpopular and therefore impracticable in civilian work.

Perhaps the use of lipovaccines will do more to solve the problem than any other factor. Le Moignic and Pinoy were the first to substitute oils for the physiologic sodium chloride solutions previously used in making vaccines, and the advantages of the change were obvious. Bacterial toxins and even endotoxins, to a degree, are lipotropic; and the fact that their toxic effects are inhibited when they are injected simultaneously with lipoids and lipoid-rich tissues, such as brain substance, has been explained on this basis. The lipoid-oil vehicle of the vaccine serves, therefore, not only in delaying absorption but very probably in some directly neutralizing manner. Indeed, Le Moignic and Pinoy found that they could inject three and four times the dose of the usual saline vaccine at a single injection of the lipovaccine without undue reaction and achieve an immunity that was on a par with that obtained following repeated inoculations with ordinary vaccines. The fact that bac-

<sup>1</sup> Reprinted from *Jour. of the American Med. Assoc.*, May, 1919.



terial vaccines prepared in oil do not deteriorate is also of decided value when mass vaccination is under consideration.

A lipodysentery vaccine has already been produced at the Army Medical School, and recently Fennel prepared a lipopneumococcus vaccine which, because of the simplicity of inoculation, will perhaps supersede the method of inoculation recommended by Lister.

An interesting application has been made, too, by Bossan and Le Moignic with a lipotuberculin. They find that such vaccines, containing either the complete suspension of tubercle bacilli or the filtered product of the dissolved material, are efficient as antigens and at the same time quite innocuous, so far as local and general reactions are concerned.

Of course, a number of technical problems have presented themselves in the mass production of these vaccines—matters of dosage and of the proper sterilization of oils, and the inclusion of efficient preservatives and antiseptics (all of our common agents are lipotropic and therefore of lessened bactericidal power in an oil menstruum), and their sale in interstate commerce has so far not been authorized by our government—but there seems little doubt that within a few years the use of lipovaccines will be of great assistance in prophylactic inoculation against a number of infectious diseases, a procedure which so far has been delayed because of the inherent toxicity of the available vaccines.

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### CHLORAMINE-T AS AN INTESTINAL ANTISEPTIC.<sup>1</sup>

The high antiseptic power and feeble toxicity of chloramine-T has suggested to P. Carnot and Th. Bondouy<sup>2</sup> the possibility of its use as an intestinal antiseptic. They report an elaborate investigation as to (*a*) its bactericidal action, (*b*) its toxic action, (*c*) its reaction with the digestive juices, (*d*) the best method for its administration; and they report a series of clinical researches on its use internally.

*Bactericidal Action.*—The bacilli of typhoid and paratyphoid are destroyed in twenty-four hours in a concentration of 1:5,000; the colon bacillus forms no culture at 1:1,000, while weaker concentra-

<sup>1</sup> Reprinted from *The Prescriber*, April, 1919.

<sup>2</sup> *Paris Med.*, 1918, 8, 468, Dec. 7.

tions are cultivated with difficulty on bouillon. The solution has no effect on *Entamoeba histolytica*.

*Toxic Action.*—This is very slight indeed, and the drug may be prescribed without fear in quite large doses even for patients having a sensitive digestive tract.

*Reaction with Digestive Secretions.*—In contact with the saliva, chloramine-T is partially decomposed with liberation of small quantities of chlorine, but this decomposition is slow and may be disregarded. The gastric and duodenal juices both decompose the drug rapidly and completely, consequently it is necessary in administration to protect the medicament from the action of the stomach. The action of both gastric and pancreatic juices is inhibited by chloramine-T in a concentration of 1 : 500, but is not affected by 1 : 2,000.

*Methods of Administration.*—In accordance with these findings it is necessary so to administer chloramine-T as to reduce the rate of its absorption and prolong its contact with the intestinal contents. The authors find that animal charcoal satisfactorily accomplishes this, cachets or tablets containing chloramine-T 0.05 Gm. and powdered animal charcoal 0.3 Gm. being a suitable form, four such cachets or tablets being given daily. Another suitable adjuvant is powdered agar-agar, this being mixed in the same proportion as the charcoal.

Clinical research shows that in cases of gastric disturbance characterized by fetid stools and diarrhoea, the administration of 3 to 6 grains produces marked relief. Bacillary dysentery was quickly relieved with two doses of 0.12 Gm. Good results were also obtained in several cases of intestinal toxic infections, and in two cases of catarrhal icterus deodorization of the stools was complete, but the icterus was unaffected. In cases of chronic enterocolitis little result was obtained, and none in cases of amoebic dysentery. In one case of paratyphoid fever the result was inconclusive.

NOTE ON THE PREPARATION OF GLYCERIN BY  
FERMENTATION.<sup>1</sup>

Karl Schweizer has explained his experiments which led to a greatly increased yield of glycerin during the fermentation of sugar by yeast, and states that during the recent war certain of the belligerent countries have prepared their glycerin industrially by this method. As early as 1857 Pasteur found that glycerin was formed during alcoholic fermentation, and he obtained a yield of 3.60 to 3.64 parts for 100 parts of sugar fermented. Later it was found by Laborde that the quantity of glycerin formed varies with different races of yeast, and obtained as much as 7.75 Gm. from 100 Gm. of sugar. It has been found also that the amount of glycerin formed is greater in a medium rich in nutritive matters, and less in cases where the conditions are less favorable for the growth of the yeast plant. It was evident that the amounts of ethyl alcohol and glycerin were not proportional.

It was supposed by T. Erlich that glycerin could be formed from certain acid amines, as is the case with amyl and other higher alcohols, and thus its formation was attributed to the fatty matter that is found in little droplets in the yeast cells, but it was demonstrated later that the quantity of this fat was too small to explain the formation.

Oppenheim proved that glycerin can be formed by the reduction of glycerin aldehyde and of dioxyacetone, substances that are formed during alcoholic fermentation, and various hypotheses were made in regard to the intermediate products of the transformation of sugar into alcohol. It appeared plausible to the author that the use of reducing agents in the fermenting liquid might increase the yield of glycerin, and accordingly experiments were made, both in his laboratory and upon a technical scale. The greatest difficulty was to find a race of yeast that would withstand the conditions, but this was found in a commercial pressed yeast made from molasses. Powdered zinc in dilute sulphuric acid solutions did not give satisfactory results, and attempts with acid solutions were abandoned. The reduction in solutions as nearly neutral as possible by means of sodium sulphite in the presence of powdered chalk was studied

<sup>1</sup> *Helvetica Chimica Acta*, 2, 167. Reprinted from *Amer. Jour. of Science*, May, 1919.



and finally led to success, after the proper concentration of the sugar solution, the amounts of sulphite and nutrients had been determined.

After dissolving 40 Gm. of sugar, 2 Gm. of ammonium biphosphate and 1 Gm. of dipotassium phosphate in 400 Cc. of water, then adding 10 Gm. of pressed yeast, the beginning of the fermentation was awaited, and then sodium sulphite to the amount of 30 Gm. was added. After twenty-four hours the fermentation was finished, 800 Cc. of carbon dioxide had been given off, the liquid had a strong odor of vanillin, and 100 Gm. of sugar had produced 21.3 Gm. of glycerin as an average of several experiments.

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## THE 98TH ANNUAL COMMENCEMENT EXERCISES OF THE PHILADELPHIA COLLEGE OF PHARMACY.

The interesting services commemorating the 98th Annual Commencement of the Philadelphia College of Pharmacy were observed during the first week in June. The baccalaureate service was held at the Church of St. Luke and the Epiphany on Sunday afternoon, June 1, the faculty and the graduates attended garbed in caps and gowns. The Rev. David M. Steele preached an enlightening and appropriate sermon.

The annual meeting of the Alumni Association was held at the college on Monday following. The officers elected for the ensuing year are: President, R. P. Fischelis; First Vice-President, Wm. D. Robinson; Second Vice-President, R. T. Blackwood; Recording Secretary, Jos. W. England; Corresponding Secretary, M. M. Smith; Treasurer, C. Carroll Meyer; Directors, E. H. Hessler, Ivor Griffith, J. W. Ehman, L. Gershenfeld, H. W. Youngken.

The faculty reception and dinner to the graduates was held in the college hall on the evening of the same day.

The Victory Reunion and Banquet of the Alumni Association took place at the Hotel Walton on Tuesday evening, June 3, and was one of the largest gatherings of the Alumni that ever assembled at these annual occasions. Dean LaWall was toastmaster and the following toasts were responded to: "The College Officers and Faculty," by Dr. A. W. Miller, who filled this assignment to President Howard B. French, whose attendance was prevented by illness;

"The Future of the College," by George M. Beringer; "The Soldier and Sailor Pharmacists," by Prof. Julius W. Sturmer; "The Navy," by Lieutenant W. T. Minnick, M.D.; "The Graduating Class," by President Otto L. Koenig, and "The Fours and Nines," by members of these special reunion classes.

The 98th Annual Commencement exercises were held at the American Academy of Music on Wednesday evening, June 4. President Howard B. French conferred the degrees and certificates.

The honorary degree of master of pharmacy, Ph.M., was conferred upon Harry Vin Army, Ph.G., Ph.D., of New York; William August Puckner, Ph.G., Phar.D., of Chicago, and Heber Wilkinson Youngken, Ph.G., Ph.D., of Philadelphia.

The following degrees and certificates were awarded to the students in the courses.

## DOCTOR IN PHARMACY (P.D.).

Name.	Thesis.	Wherefrom.
Hess, Mrs. Helen Way (P.C.)	<i>Organotherapy</i>	New Jersey.

## PHARMACEUTICAL CHEMIST (PH.C.).

Braslavsky, Albert	<i>Sodium Salicylate</i>	Pennsylvania.
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## GRADUATE IN PHARMACY (PH.G.).

Name.	Thesis.	Wherefrom.
Abrahams, Samuel	<i>Elixir Terpin Hydrate</i>	Pennsylvania.
Altshuler, Samuel Benson	<i>Linimentum Calcis</i>	Russia.
Baker, Benjamin	<i>Gossypium Purificatum</i>	Pennsylvania.
Baker, John Luther	<i>Colloids</i>	Pennsylvania.
Berguido, Luis	<i>Adulteration of Matricaria</i>	
	<i>Chamomilla by Anthemis Cotula</i>	Panama.
Blackwood, Russell Thorn, Jr.	<i>Perfumery</i>	Pennsylvania.
Bloes, Walter Franklin	<i>American Grown Belladonna</i>	Pennsylvania.
Buchanan, Raymond Joseph	<i>Incompatibility in Prescriptions</i>	Pennsylvania.
Collins, Amos Reeves	<i>Notes on Arnica Montana</i>	Pennsylvania.
Dixon, Hayes Merrill	<i>Starch Grains of Leguminosæ</i>	
	<i>Family</i>	Pennsylvania.
Dorin, David	<i>Development of the Potassium</i>	
	<i>Industry in the United States</i>	Russia.
Emig, Herbert Martin	<i>Enteric Pill Coating</i>	Pennsylvania.
Eppley, Joseph Aloysius	<i>Preparations of Dichloramine-T</i>	Pennsylvania.
Fasnacht, Allen Hornberger	<i>Liquor Magnesii Citratis</i>	Pennsylvania.
Finkeni, Paul William	<i>Disinfectants and Their Uses</i>	New Jersey.
Friedman, William Leonard	<i>Manna and Mannite</i>	Pennsylvania.

- Goldin, Joseph Bernard .... *Eusol and Eupod* ..... Russia.  
 Hellerman, Edward Mann .. *The Use of Iodine in Treatment  
of Pyorrhea* ..... Pennsylvania.  
 Henrie, John Lewis ..... *The Cultivation of the Mushroom  
Commercially* ..... Pennsylvania.  
 Hoy, Wilbur Bloom ..... *The Characteristics of Angostura  
and Surinam Tonka Beans* ... Pennsylvania.  
 Hughes, John Joseph ..... *The Histology of Xanthoxylum* . Pennsylvania.  
 Hurst, George A. .... *Pollen Extracts and Their Use* .. Pennsylvania.  
 Josephs, Aaron Harry ..... *Purified Petroleum Benzin* .... Pennsylvania.  
 Katsky, Jacob Herman ..... *Camphor and its Polariscopeal  
Determination* ..... Russia.  
 Kiely, Eugene Ignatius ..... *Seidlitz Powder* ..... Pennsylvania.  
 Koenig, Otto Louis, Jr. .... *Pharmaceutical Technique* ..... Pennsylvania.  
 Koffs, Joseph ..... *Pulverization of Boric Acid* .... Pennsylvania.  
 Levin, Miss Sarah ..... *The Peppermint Industry* ..... Pennsylvania.  
 Liss, Miss Ethel ..... *Aerial or Gaseous Disinfection* .. Pennsylvania.  
 McClure, Maurice Axe .... *Eupatorium Perfoliatum* ..... Pennsylvania.  
 Mayer, Harry Oscar ..... *Digitalis Siberica* ..... Pennsylvania.  
 Meserofsky, Jacob ..... *Diphtheria Antitoxin* ..... Russia.  
 Molofsky, David ..... *The Quality of Drugs of Ameri-  
can Manufacture* ..... New York.  
 Moyer, Lloyd Rickert ..... *Adonis Vernalis* ..... Pennsylvania.  
 Pachuta, Michael ..... *Tablet Triturate Bases* ..... Pennsylvania.  
 Pinsky, Miss Harriet  
   Floren ..... *Soy-Beans* ..... Pennsylvania.  
 Posnansky, Maurice Albert . *Drug Store Advertising* ..... Russia.  
 Price, Samuel Howard .... *Passiflora Incarnata* ..... No. Carolina.  
 Promisloff, Israel Samuel .. *Disadvantage of Sodium Bicar-  
bonate Tablet in Liquor Mag-  
nesii Citratis* ..... Russia.  
 Randolph, John Roanoke .. *Scutellaria and Its Substitutes* .. Tennessee.  
 Reighter, William Erle .... *Cocoanut Products* ..... Pennsylvania.  
 Reiter, George Hager ..... New Jersey.  
 Rodriguez, Pedro Manuel,  
   Oquendo ..... *Carica Papaya* ..... Cuba.  
 Rohrbach, George William.. *Ipecacuanha* ..... Pennsylvania.  
 Sanders, Miss Annetta  
   Mildred ..... *Bird Foods* ..... Maryland.  
 Scott, William Clement .... *Paste* ..... Pennsylvania.  
 Seltzer, Joseph Pincus .... *Serums and Vaccines* ..... Russia.  
 Silk, Jacob ..... *Ferrous Iodide in Syrup* ..... England.  
 Slipakoff, Samuel Albert ... *The Olive and Its Oil* ..... Pennsylvania.  
 Smith, Albert H. .... Pennsylvania.  
 Smith, Marcus Samuel .... *Sterilization of Camphorated Oil* . Pennsylvania.  
 Springer, Altha Raymond .. *The Clinical Laboratory of the  
United States Army* ..... Pennsylvania.  
 Stam, Miss Lillian Roberts . *Water Softening* ..... Maryland.



Trumbower, Russell Stanley	<i>Carrel-Dakin Solution</i>	Pennsylvania.
Ulmer, Albert Herman	<i>Extemporaneous Pill Coatings</i>	Pennsylvania.
Waidelich, Harold Russell	<i>Lobelia Inflata</i>	Pennsylvania.
Wallace, John Aloysius	<i>Milk as a Clarifying Agent</i>	Pennsylvania.
Weinberg, Isadore Binder	<i>Examination of Commercial Samples of Acetyl Salicylic Acid</i>	Pennsylvania.
Williams, Daniel Thomas	<i>Salvia Lavandula Folia Substituted for Salvia Officinalis</i>	Pennsylvania.

## CERTIFICATE OF PROFICIENCY IN CHEMISTRY.

Name.	Wherefrom.
Cunningham, Henry M.	Pennsylvania.
Dickhart, Wallace H.	Pennsylvania.
Feeny, Leonard A.	Pennsylvania.
Sunshine, Abraham J.	Pennsylvania.

## SPECIAL CERTIFICATE IN ANALYSIS OF OILS, SUGAR AND WATER.

Duster, Elmer J., P. D.	Pennsylvania.
Nunez, Manuel Francisco	Peru.

## SPECIAL CERTIFICATE IN CHEMICAL URINALYSIS.

Barreras, Fernando, Ph.G.	Porto Rico.
Nunez, Manuel Francisco	Peru.

## SPECIAL CERTIFICATE IN COSMETICS AND PERFUMES.

Tamura, Sokichi	Japan.
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## CERTIFICATE IN BACTERIOLOGY.

Barreras, Fernando, Ph.G.	Porto Rico.
Beechwood, Miss Mary Elizabeth, Ph.G.	Pennsylvania.
Coolbaugh, Leonard E., P.D.	New York.
Dixon, Herbert Carlyle	Pennsylvania.
Glantz, Morris, Ph.G.	Russia.
Green, Samuel	Pennsylvania.
Griggs, Miss Anna Mae	Pennsylvania.
Londa, Miss Lena	Pennsylvania.
Luongo, Guy R., Ph.G.	New Jersey.
Mayer, Harry O.	Pennsylvania.
Nace, Earl Gray, P.D.	Pennsylvania.
Nunez, Manuel Francisco	Peru.
Ott, Miss Pearl M.	Pennsylvania.
Rodriguez, Pedro M.	Cuba.
Roth, Herbert J.	Pennsylvania.
Shute, Joseph, Ph.G.	Pennsylvania.
Smith, Marcus Samuel	Pennsylvania.
Stephens, Stanley R.	Pennsylvania.
Stock, Roy A., Ph.G.	Pennsylvania.
Weidman, Isaac S.	Pennsylvania.

Wells, Miss Eleanor H. ....	Pennsylvania.
Whalen, Miss Margaret R. ....	Pennsylvania.
Zajkowski, Anthony, Ph.G. ....	Pennsylvania.

SPECIAL CERTIFICATE IN TECHNICAL MICROSCOPY.

Nunez, Manuel Francisco .....	Peru.
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CERTIFICATE IN PHYSIOLOGIC ASSAYING.

Name.	Wherefrom.
Cook, E. Fullerton, P.D., Ph.M. ....	Pennsylvania.
Harvey, Gilbert L. ....	Pennsylvania.
Goinez, LeRoy H. ....	Ohio.
Mayer, Harry O. ....	Pennsylvania.
Worrall, Wesley .....	Pennsylvania.

CERTIFICATE OF ATTENDANCE AT THE UNITED STATES NAVAL HOSPITAL CORPS  
TRAINING SCHOOL OF THE PHILADELPHIA COLLEGE OF PHARMACY,  
SECOND UNIT.

Name.	Town.	State.
Barker, Ernest Milton .....	Roseburg .....	Oregon.
Brandt, Frederick Eugene .....	St. Louis .....	Missouri.
Carlisle, John Edward .....	Washington .....	Pennsylvania.
Daube, Charles Frederick W. ...	Philadelphia .....	Pennsylvania.
Gilson, Howard Burbank .....	Edgewood .....	Pennsylvania.
Hale, Will Norris .....	Rockdale .....	Texas.
Hunt, Jesse Hamblet .....	Sisquoc .....	California.
Jones, John Edmund .....	Douglas .....	Arizona.
Kyner, John Harvey .....	Eustis .....	Nebraska.
Lee, Vernon .....	Stigler .....	Oklahoma.
Morris, Herbert Reed .....	Las Animas .....	Colorado.
Nevans, David Harold .....	Denver .....	Colorado.
O'Neill, Charles Henry .....	Webb City .....	Missouri.
Rathke, Arnold Leander .....	San Antonio .....	Texas.
Ryan, Charles Augusta .....	Portland .....	Oregon.
Sheppard, Allen Charles .....	Haleyville .....	New Jersey.
Shytles, Harrie Marcellus .....	Venus .....	Texas.
Stovell, George Reynolds .....	Caldwell .....	Idaho.
Sturgill, Virgle Leon .....	Ada .....	Oklahoma.
Taylor, Alfred Vernon .....	Denver .....	Colorado.
Traeder, Will Melrose .....	Pueblo .....	Colorado.
Waitman, Bryan Jennings .....	Redington .....	Nebraska.
Wersen, Harold Edward .....	Mt. Vernon .....	Washington.

The first Unit of Hospital Corpsmen, a class of 162 enlisted men, completed their course at the College February 15, 1919, and a large number were given certificates and advanced naval rating.

The address to the graduates was delivered by Judge John M.

Patterson, and was a masterly presentation of true Americanism and advice which followed would lead to the highest type of useful citizenship and individual success.

A notable feature on this memorable occasion was the distribution with the programmes of the "Honor Roll of Graduates and Students of the Philadelphia College of Pharmacy who served in the United States Army or the United States Navy during the Great World War." The roll included nearly five hundred names of those who are known to have performed military service during this period. Possibly there are many more, of whose service for the country, the college has not yet been advised. Taps were sounded for the list of twenty names of former students who died in the service or were killed in action.

The following is a reproduction of a bronze medal or token of appreciation that has been prepared by the college and which will be presented to each graduate or student of the college who during this war has performed military or special service for the government. The medal will be sent to the family of such as have made the supreme sacrifice.



At the commencement, President French made the speech of presentation and Robert P. Fischelis responded, accepting the honor in behalf of those who had been in the service and pledging their continued loyalty to the nation and to the college.



## NEWS ITEMS AND PERSONAL NOTES.

CASWELL A. MAYO, PH.M., REMOVES TO CINCINNATI.—Mr. Caswell A. Mayo, who for twenty-seven years has served as the editor of our esteemed journalistic contemporary, the *American Druggist and Pharmaceutical Record*, has severed his editorial connection with that journal and engaged with the William S. Merrell Company of Cincinnati.

Since his entrance as a student at the Philadelphia College of Pharmacy Mr. Mayo's career has been a series of distinguished services in behalf of the vocation that he selected for his life's work. His efforts have, from time to time, received merited recognition. His alma mater conferred upon him the degree of master of pharmacy, *honoris causa*, and the American Pharmaceutical Association elected him as president, 1914-1915. In addition, he has held many responsible positions in the New York College of Pharmacy and in the various pharmaceutical organizations. Not the least of his services to pharmacy have been the addresses and penned articles in favor of professional pharmaceutical work in the Army, Navy and Health Departments of the Federal Government with appropriate commissioned rank for pharmacists. Mr. Mayo carries with him to this new field of activities the high regards of a host of friends and their best wishes for a continuance of the high ideals that have characterized his past work and, if possible, that even greater personal satisfaction and success may attend him therein.

BURROUGHS WELLCOME MANAGER VISITS AMERICA.—George E. Pearson, F.C.S., general manager of Burroughs Wellcome & Co., London, England, is paying a visit to America and in his tours is taking in some of the interesting sights as well as calling upon friends and customers of his well-known firm. It was a pleasure to welcome him at the Philadelphia College of Pharmacy, on Tuesday, May 24, and to have him make a personal inspection of this institution.

DECEASE OF PROF. WILLIAM G. FARLOW.—On June 3, William G. Farlow, professor of cryptogamic botany at Harvard University, died at his home at Cambridge, Mass., aged 74. He was recognized as an authority in the botanical sciences, especially in the department thereof in which he had specialized and taught at Har-

vard. His publications and scientific contributions were of a high order of merit.

THE SUPREME COURT OF THE UNITED STATES SUSTAINS THE LEGALITY OF COLGATE CO.'S SELLING PLAN.—In an unanimous opinion filed on June 2 the United States Supreme Court has affirmed the judgment of the District Court of Virginia in sustaining the demurrer of Colgate Co. to the indictment brought against this firm by the Federal Trade Commission, alleging that their plan of selling was in violation of the Sherman Act, and dismissing the said complaint.

In reviewing this case the Supreme Court in the opinion states in part:

“No charge is made that any contract was entered into by and on the part of the defendant, and any of its retail customers, in restraint of interstate trade and commerce, the averment being, in effect, that it knowingly and unlawfully created and engaged in a combination with certain of its wholesale and retail customers, to procure adherence on their part, in the sale of its products sold to them, to resale prices fixed by the defendant; and that, in connection therewith, such wholesale and retail customers gave assurances and promises, which resulted in the enhancement and maintenance of such prices, and in the suppression of competition by wholesale dealers and retail dealers, and by the latter to the consuming public.

“‘The retailer, after buying, could, if he chose, give away his purchase or sell it at any price he saw fit, or not sell it at all, his course in these respects being affected only by the fact that he might by his action incur the displeasure of the manufacturer who could refuse to make further sales to him, as he had undoubted right to do.’ And we must conclude that, as interpreted below, the indictment does not charge Colgate & Company with selling its products to dealers under agreements which obligated the latter not to resell except at prices fixed by the company.

“The position of the defendant is more nearly in accord with the whole opinion and must be accepted. And as counsel for the Government were careful to state on the argument that this conclusion would require affirmation of the judgment below, an extended discussion of the principles involved is unnecessary.

"The purpose of the Sherman Act is to prohibit monopolies, contracts and combinations which probably would unduly interfere with the free exercise of their rights by those engaged, or who wish to engage, in trade and commerce—in a word to preserve the right of freedom to trade. In the absence of any purpose to create or maintain a monopoly, the Act does not restrict the long recognized right of trader or manufacturer engaged in an entirely private business, freely to exercise his own independent discretion as to parties with whom he will deal. And, of course, he may announce in advance the circumstances under which he will refuse to sell. 'The trader or manufacturer, on the other hand, carries on an entirely private business and may sell to whom he pleases.' *United States v. Trans-Missouri Freight Association*, 166 U. S. 290, 320. 'A retail dealer has the unquestioned right to stop dealing with a wholesaler for reasons sufficient to himself, and may do so because he thinks such dealer is acting unfairly in trying to undermine his trade.' *Eastern States Retail Lumber Dealers' Association v. The United States*, 234 U. S. 600, 614. See also *Standard Oil Company v. United States*, 221 U. S. 1, 56; *United States v. American Tobacco Company*, 221 U. S. 106, 180; *Boston Store of Chicago v. American Graphophone Company et al.*, 246 U. S. 8. In *Dr. Miles Medical Company v. Park & Sons Company*, *supra*, the unlawful combination was effected through contracts which undertook to prevent dealers from freely exercising the right to sell.

"The judgment of the District Court must be

*"Affirmed."*

This decision of the United States Supreme Court will undoubtedly have an important bearing upon the future course of the Federal Trade Commission and may even be considered a long step in the direction of modifying the interpretation placed upon the Sherman Anti-Trust Act or preferably its modification by legislation that will promote fair methods of trading and the restriction of unscrupulous price-cutting. The unanimity of the decision leaves no doubt as to the trend of public opinion. In an editorial comment when this suit was announced (see *AMERICAN JOURNAL OF PHARMACY*, March, 1918, page 160) the following statement was made: "It would appear to us that there is here *no evidence of intent to restrain trade*. The effort of Colgate and Company appears to be



to standardize, to stabilize prices in the interest of all concerned. The effect has been the very opposite of a restraint of trade. This plan has stimulated the interest of dealers and gained the confidence of the consumers and the actual result has doubtless been an increased consumption of the products of Colgate and Company. That such a plan, which is essentially a plan for 'fair trade,' working to the benefit of all the interests concerned, should be construed as a violation of any law enacted in the interest of fair trade appears to us as inconsistent and untenable."

ROBERT P. FISCHELIS PRESIDENT OF THE PENNSYLVANIA PHARMACEUTICAL ASSOCIATION.—At the annual meeting of this association held at Buena Vista the latter part of June, Prof. Robert P. Fischelis was elected as the president for the ensuing year. For several years past he has been the efficient secretary and editor of its proceedings and publication, *The Pennsylvania Pharmacist*.

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#### BOOK REVIEWS.

A TREATISE ON PRESCRIPTION INCOMPATIBILITIES AND DIFFICULTIES, including prescription oddities and curiosities. For pharmacists and physicians and students in pharmacy and medicine. By William J. Robinson, Ph.G., M.D., editor of the *Critic and Guide* and *The American Journal of Urology and Sexology*; formerly president of the New York Board of Pharmacy Institute, etc., 12mo, 263 pages, cloth, \$3. New York, Critic and Guide Company.

This excellent contribution to the study of incompatibilities in prescriptions will be received with interest by all pharmacists who are proud of their professional training. The collection represents many of the modern synthetics in combination, and the explanations are interestingly written, and indicate investigation by the author.

It is true, many old and well-known incompatibilities are included, as they should be in any comprehensive study of the subject, but there are a number of the new combinations and interesting complications which every practicing pharmacist should know.

The author points out a fact which is being generally recognized, namely, that physicians are writing few composite prescriptions, the

tendency being toward the use of "simples," and therefore problems in incompatibility less frequently force themselves upon the compounder. There is always great danger of over-emphasis on this subject, since the physician resents constant change in his prescription, but the master prescriptionist is frequently able to gain the confidence of his physician friends by judicious and skillful use of his scientific training and cleverness in compounding mixtures in a compatible and elegant form.

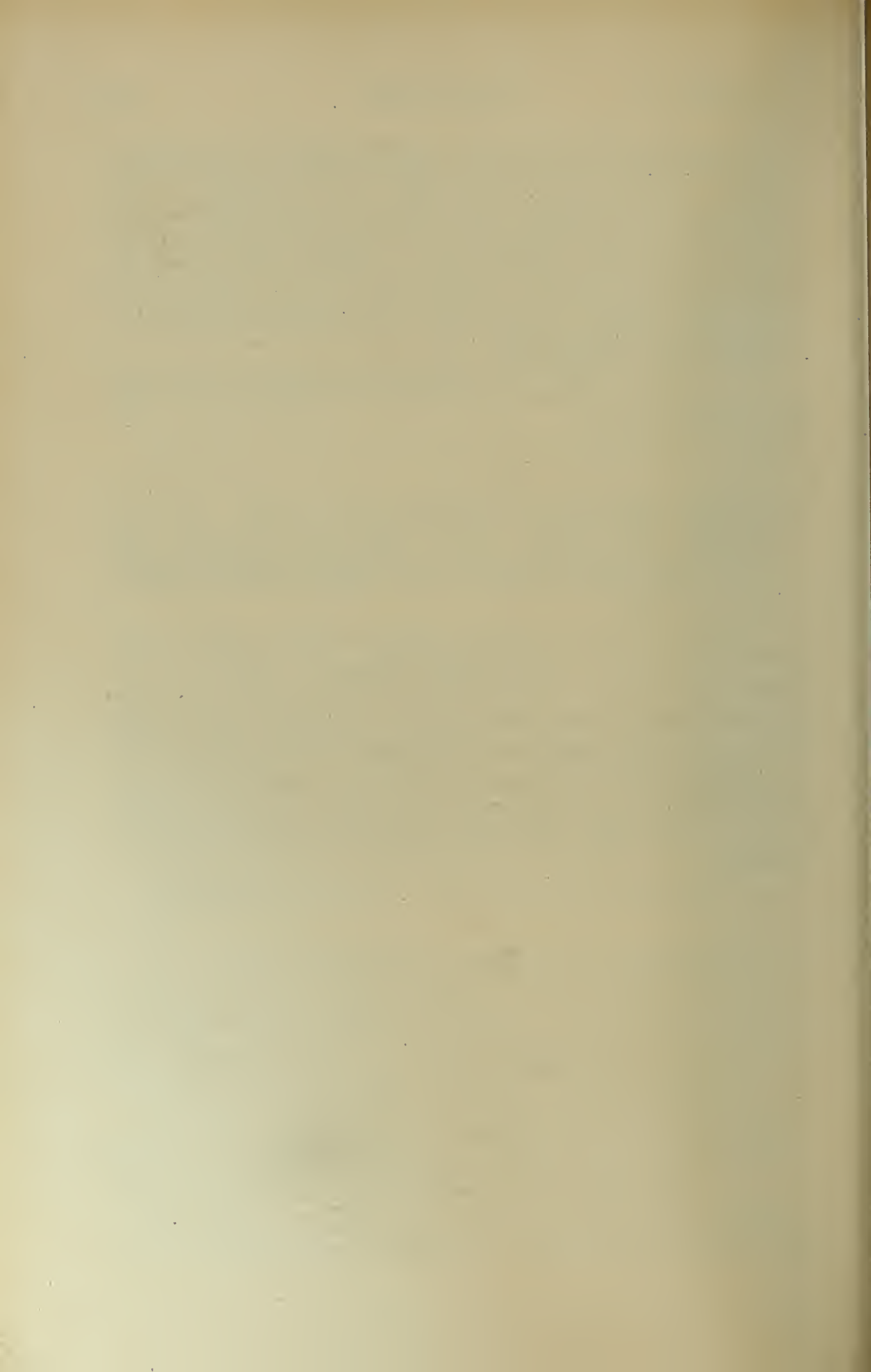
This volume should find its place in the library of every active prescriptionist and will be of great value in clearing disputed points in prescription work.

E. F. C.

A CRITICAL REVISION OF THE GENUS EUCALYPTUS. By J. H. Maiden, I.S.O., F.R.S., F.L.S., Government Botanist, New South Wales, and Director of the Botanic Gardens, Sydney. Vol. IV, Part 7.

The part 7, Vol. IV, being part XXXVII of the complete work, now at hand carries on this classic monographic treatment of the interesting Eucalypti, in the same manner and style as the preceding parts which from time to time have been reviewed in these pages. The species treated therein are *E. clavigera* A. Cunn with the various affinities and connecting varietal types; *E. aspera* F. v. M.; *E. grandifolia* R. Br.; *E. papuana* F. v. M. The excellent illustrations are of the same high order that appeared in all of the parts as published.

G. M. B.





# THE AMERICAN JOURNAL OF PHARMACY

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AUGUST, 1919

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## EDITORIAL.

### PROPRIETIES IN ADVERTISING.

The address of Mr. Burwell S. Cutler on "Commercial Ethics," reprinted in this number of the AMERICAN JOURNAL OF PHARMACY, is but another evidence of the moral code that is becoming more thoroughly developed and more firmly established in the business world. The thoughtful and progressive merchant, whether engaged in foreign or in domestic commerce, must have observed the improved moral tone, the distinct advancement of ethical principles, the elevation to a higher plane that has marked the recent trend of thought and actions of business men. This is equally true of those associated with large enterprises, the men of big business, as well as those associated with merchandising in a retail way or in comparatively small industries. It appears as another hopeful sign of the community of interests, the brotherhood of men, and the practical application of the golden rule.

It may be true that, to a certain extent, and especially in certain trades, the changes noted are traceable to compulsion, the constraining influences of certain legal enactments such as the Food and Drugs Act, the Sherman Anti-trust Law, and The Federal Trade Commission Act. Without minimizing in the least, the educational and moral effect that these acts and their application may have had in correcting certain trade evils, the writer is of the opinion that the great determining factor of the moral uplifting of business is the growth of the American ideals of fairness, of uprightness, and justice. The majority of American merchants need no law to teach them the principles of honorable dealings and would scorn the statement that the old adage "caveat emptor" had any relation to or significance in their trade.

One of the encouraging signs of the times and of the sensitiveness of trade organizations to the ethics of commerce, is the promptness with which any digression from either the unwritten law or the established rules of "fair trade" is recognized and objected to.

An incident that well illustrate this point was the action taken at the recent annual meeting of the Pennsylvania Pharmaceutical Association in the unanimous adoption of the following resolutions.

WHEREAS the Bayer Company, proprietors of Bayer's Aspirin tablets, is making a practice of publishing advertisements in the daily papers of this country in which the following statements appear:

"Don't Buy Aspirin in a Pill Box."

"Fake Aspirin was Talcum," underneath which appears the picture of a man holding his hand up to the druggist and saying, "You can't hand me any substitute for the true, genuine Bayer's Aspirin" which statement is followed by a question: "Haven't you heard?" "A Brooklyn Fraud is in jail for flooding the country with millions of counterfeit tablets. He labeled them Aspirin, but they were Talcum Powder!" and

WHEREAS the apparent object of these advertisements is to plant in the public mind the belief that every druggist who sells other brands of aspirin than Bayer's is dishonest, which, if this belief should become fixed in the public mind permanently, injurious results would be produced to the business of retail druggists, therefore be it

*Resolved*, that the Pennsylvania Pharmaceutical Association in regular annual meeting assembled, does hereby most earnestly protest the employment of such advertising and calls upon the Bayer Company to henceforth refrain from publishing the advertisements herein objected to or any others which tend to discredit the retail druggist in the public mind, and

*Resolved*, that the members of this association should refuse to sell any more Bayer Aspirin Tablets than are called for so long as the Bayer Company persists in employing such outrageous and insulting advertisements, on the ground that the Bayer Company does thereby place the distribution of its products outside the channels of self-respecting and honest druggists, and be it still further

*Resolved*, that a copy of these resolutions be sent immediately to the Bayer Company, and to each state pharmaceutical associa-

tion with the request that the latter take action and protest against the aspersion cast on all retail druggists by the Bayer Company through the aforesaid advertising."

An advertiser is justified in extolling the virtues of his own product and by every legitimate means endeavoring to command the attention of the public to the article that he is commending. He is not warranted, however, in his advertisements in decrying the products or in defaming the character of his competitors. The proprieties of advertising are being evolved and the advertising pages of our leading journals and magazines give evidence of the improvement in taste and the ethics of business that mark this phase of commercial enterprise.

The AMERICAN JOURNAL OF PHARMACY has rigidly maintained its standard and questionable advertisements have been censored or declined, and we believe that our strict adherence to the proprieties that should be observed in the advertising pages of an ethical and scientific journal as well as in its editorial columns and published articles, has added materially to the recognized standing of the JOURNAL and the value of its service to its advertising patrons.

The advertisement that was so properly objected to by the Pennsylvania pharmacists is the same obnoxious style that some twenty years or so ago, was very extensively employed by the representatives of certain German patented medicinal chemicals in foisting their products upon the American consumers at fabulous prices.

It was particularly objectionable because of its wide publicity in the newspapers of the country, thus spreading before thousands of readers a reflection upon the druggists of the country; an aspersion that was not applied to any persons who may have engaged in the criminal practice referred to in the advertisement, but gave the impression that it was applicable to the entire vocation of pharmacy. It is exceedingly unfortunate that the American firm who, by virtue of the sale of the German-controlled company by the Alien Property Custodian succeeded to this business, should have committed the error of continuing the Hun method of advertising.

As a corollary of our proposition that there has developed a distinct code of ethics among our business men and that this is progressive and is founded upon principles of honor and upright-



ness we are pleased to publish the following quotation from the reply of the Bayer Company, Inc.

"We are naturally very sorry to learn that your organization has taken exception to some of our recent advertising, and we take pleasure in informing you that the particular copy complained of has been discontinued. It is unnecessary to say that we are desirous of retaining the good will of all retail druggists, as we recognize the fact that they are a necessary link in the chain of distribution of our merchandise, and we consider their interests as identical with our own.

"In our opinion no class of business men are more deserving of the respect of the public, but we feel sure that you will agree that there are exceptions to this rule. This is made evident by the fact that the president of the Verandah Chemical Co., of Brooklyn, who manufactured and marketed what they chose to call 'Aspirin,' was recently sentenced to the penitentiary because his company had been shown to have sold hundreds of thousands of tablets consisting entirely of talcum powder.

"The evidence in the case showed that sales of this material had been made throughout the United States, and while we are loathe to believe that these were purchased by the better class of druggists, the quantities involved were so considerable that we were convinced some action on our part was absolutely essential. It seemed to us therefore that we were morally obligated to call the attention of the public to this incident, and to warn them accordingly, and we feel certain that every member of your association would have acted similarly under the same circumstances.

"We sincerely trust that upon further reflection you will believe that we were absolutely justified, and assuring you of our desire to assist the legitimate drug trade in every possible way."

This admission of their error in deviating from the proprieties of advertising, while not as frank as we might wish, is nevertheless an admission accompanied by an explanation, which showed a just cause for their resentment against certain rascals but which could not justify a disparagement of the entire drug trade. We are of the opinion that the present management of this company is composed of fair-minded American business men and the discontinuance of this style of advertisements evidences that the ethics of business and the properties of advertising will be observed by

them in the future. We congratulate the pharmacists of Pennsylvania for having the courage of their convictions and on the timely action taken.

G. M. B.

## A FURTHER RULING RELATING TO EXEMPTED NARCOTICS.

Under date of July 30, the following letter was received from the office of the Commissioner of Internal Revenue. As it sets forth the position of the department on trading in "exempted narcotics" and the records to be kept by dealers therein, the information contained is important to the drug trade and by permission of the recipient is published for the guidance of druggists.

"Receipt is acknowledged of your letter of the second instant, in which you ask for information relative to the registration in Class 5 under the Harrison Narcotic Law, as amended, of manufacturers and dealers in preparations and remedies exempt under Section 6, as amended.

In reply you are advised that manufacturers of exempt preparations are required to register in Class 5 and pay special tax of \$1 a year or fraction thereof. Registration in this class entitles persons so registered to purchase order forms upon which to secure the narcotic drugs entering into the manufacture of their product. Class 5 registrants will not be required to make or file an inventory of exempted drugs.

Every manufacturer, producer, compounder, or vendor (including dispensing physicians) of exempt preparations or remedies must keep a daily record of all sales, exchanges, or gifts of such preparations or remedies.

The record to be kept by manufacturers, producers, or compounders of, and wholesale dealers in untaxed narcotic preparations or remedies must show the date of sale, registry number of person to whom sold, the name and address of the purchaser and the name and quantity of preparation or remedy sold, exchanged or given away. An accurate record must also be kept by manufacturers, producers and compounders of drugs purchased by them on order forms and used in the production of exempted preparations or remedies showing the date when a new mixture is made up, the name and quantity of the particular narcotic drugs used and the date when the mixture is exhausted.

Retail dealers must keep a daily record of narcotic drugs dispensed showing the rate of sale, signature of purchaser, address of purchaser and name and quantity of the preparation or remedy sold. The record of untaxed narcotic drugs sold on prescriptions must show the quantity of drug, name of drug, serial number of prescription, and name and address of person to whom sold. Prescriptions calling for exempted narcotic preparations or remedies must be kept on a separate file.

The government will not furnish blanks upon which to keep these records.

All entries on the daily record must be made at the time of sale.

### ANOTHER STEP TOWARD PRICE MAINTENANCE.

In commenting on the recent decision of the United States Supreme Court in the "Colgate Case" (*AMERICAN JOURNAL OF PHARMACY*, July, 485) the opinion was expressed "That this decision will undoubtedly have an important bearing upon the future course of the Federal Trade Commission and may even be considered a long step in the direction of modifying the interpretation placed upon the Sherman Anti-Trust Act or preferably its modification by legislation that will promote fair methods of trading and the restriction of unscrupulous price-cutting." This prediction has been verified even more quickly than we dared to hope for.

In a special report to Congress the Federal Trade Commission (on July 12) renewed its recommendation made last December that manufacturers be permitted by law to fix and maintain resale prices, subject to review by a disinterested agency.

The commission says that such a law would remove present complexity in the business world, promote the efficiency of manufacturing and commercial institutions and serve the interest of the consuming public.

Under the commission recommendation, manufacturers desiring to fix and maintain resale prices would file with an agency to be designated by Congress, descriptions of their articles, contracts of sale, and the price schedules to be maintained. The disinterested agency would be charged with the duty, "upon complaint of any dealer or consumer or other party at interest," to review the terms of contracts and prices.



The commission's recommendations, it stated, were based on the following conclusions:

1. That producers of identified goods should be protected in their intangible property right or good-will, created through years of fair dealing and of sustained quality of merchandise;

2. That the unlimited power both to fix and to enforce and maintain resale prices may not be made lawful with safety; and

3. That unrestrained price-cutting is not in the public interest, and tends, in the long run, to impair, if not to destroy, the production and distribution of articles desirable to the public.

"There must be a common ground," the commission said, "wherein the rights of producer, purveyor and consumer may each be fully secured and equity done to all. The search for such a ground has been a task of the commission."

The text of the commission's special report to Congress follows:

"The Federal Trade Commission under paragraph (f), Section 6 of the Federal Trade Commission Act, addresses the Congress by way of a special report designed to direct attention to the subject of control of resale prices by the manufacturers of a class of articles in interstate commerce.

"The question is, whether or not a manufacturer of standard articles, identified either by trade-mark or trade practice, should be permitted to fix by contract, express or implied, the price at which the purchaser can resell them.

"The question has been continuously before the commission since its creation. It has been the subject of study, investigation and hearing and constantly recurs, in various forms, in complaints filed with the commission by business concerns.

"The Supreme Court has made it clear that, in the present state of the law, the maintenance of a resale price by the producer, is a restraint of trade and is unlawful.

"Such being the judgment of the Supreme Court, the Federal Trade Commission has enforced the law, even though it may have appeared to operate inequitably in some cases. In its enforcement of this rule, the commission has been mindful that the cutting of a recognized resale price on well established and identified articles has been, at times, indulged in for unfair trade purposes. When so unfairly used, such price cutting is attempted to be cloaked as lawful competition and justified by the Supreme Court decisions.

"Thus, both price maintenance, and price cutting under certain conditions, are found to be unfair and business men are perplexed. It is with the desire that this perplexity may be terminated that the commission addresses the Congress.

"It is urged, and, the commission believes, with reason, that it would be unwise to vest with the manufacturers of articles the right, without check or review, both to fix and to compel the maintenance of resale prices. It is true that business practice inclines producers to fix the lowest possible retail price in order to secure the greatest possible sale of their product, but in the complex commercial organism functioning between the production of an article and its final sale, for actual consumption, both the wholesale and retail merchant are entitled to just compensation for useful service performed.

"It is similarly urged, that manufacturers should be protected in their good will created by years of fair dealing and of sustained quality of merchandise.

"The consuming public does not enjoy benefits by unfair price cutting to compensate it for the injuries following demoralization caused by price cutting. This for the reason that, in the long run, unrestrained price cutting tends to impair, if not to destroy, the production and distribution of articles desirable to the public.

"There must be a common ground wherein the rights of producer, purveyor and consumer may each be fully secured and equity done to all. The search for such ground has been a task of the Commission and results in the following conclusions: (1) That producers of identified goods should be protected in their intangible property right or good-will. (2) That the unlimited power both to fix and to enforce and maintain a resale price may not be made lawful with safety. (3) That unrestrained price cutting is not in the public interest.

"Bills now pending before Congress may well be made to meet the difficulties of the situation if amended to provide for a review of the terms of resale contracts and a revision of resale prices, by a disinterested agency.

"Therefore, it is recommended that it be provided by law that if the manufacturer of an article produced and sold under competitive conditions, desires to fix and maintain resale prices, he shall file with an agency designated by the Congress, a description of such article, the contract of sale and the price schedule which he pro-

poses to maintain, and that the agency designated by the Congress be charged with the duty, either upon its own initiative or upon complaint of any dealer or consumer or other party in interest, to review the terms of such contract and to revise such prices and that any data and information needful for a determination be made available to such agency.

"Such legislation would seem to be in accord with the spirit of the times in that it is designed, by removing this perplexity, to promote the efficiency of manufacturing and commercial institutions and so to serve the interest of the consuming public.

The commission respectfully renews its recommendation of December 2, 1918. The conditions surrounding the fixing and enforcement of the maintenance of resale prices have not materially changed since this recommendation was made. The recent decision of the Supreme Court in *United States v. Colgate & Co.* has not apparently legalized contracts providing for the maintenance of resale prices, as the court expressly stated that the indictment did not charge the existence of contracts in that case, and distinguished it from the case of *Dr. Miles Medical Co. v. Park & Sons* on that ground. If the decision be construed to hold it lawful, under the Sherman Law, for manufacturers to fix resale prices and to enforce the maintenance of such prices by refusal to sell to those who do not resell at the prices fixed, or by other means, it does not follow that the fixing and enforced maintenance of such prices is not an unfair method of competition within the meaning of Section 5 of the Trade Commission Act. In order to establish a violation of the Sherman Anti-Trust Act a contract, combination or conspiracy must be proven. If some device for restraining trade be devised which does not fall within the definitions comprehended by these three terms as construed by the courts, it does not constitute a violation of the act, though restraint of trade may result.

"The enforcement of resale prices on goods in the hands of distributors is identical in its effect upon dealers and the public, whether it be accomplished by contract, combination or conspiracy, or by some other means. An unfair method of competition within the meaning of Section 5 may involve the use of contracts or the formation of combinations or conspiracy, but neither of the three is necessary to establish a method of competition. Indeed, unfair methods of competition do not ordinarily involve such contracts or conspiracies. The effect of price maintenance being the same how-



ever accomplished, it may well be urged that such a method of competition violates Section 5 of the Commission Act since it prevents distributors, wholesale and retail, from engaging in price competition on such goods after they have passed into their hands and deprives the public of the benefits of competition in the distribution of all such goods.

"It might also be urged that when price maintenance is approached from the standpoint of an unfair method of competition, regard must be had to its effect when employed by many manufacturers rather than when employed by one, and that in this view it results in the elimination of price competition in the distribution on a vast and constantly increasing number of commodities of common necessity.

"On the other hand, if the effect of the Colgate decision be to legalize the fixing and the enforcement of the maintenance of resale prices other than by contract, the desirability of the enacting of legislation recommended by the commission becomes even more apparent. In the commission's previous report it was stated that the unlimited power both to fix and enforce the maintenance of resale prices may not be made lawful with safety to the public. The interest of the consuming public in the enacting of such legislation is therefore more vital at this time than when recommendation was previously made.

"WILLIAM B. CLOVER,  
"JOHN FRANKLIN FORT,  
"VICTOR MURDOCK,  
"HUSTON THOMPSON,  
*Commissioners.*"

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## NOTES ON THE DASHEEN AND CHAYOTE.<sup>1</sup>

BY HEBER W. YOUNGKEN, PH.D.,  
PHILADELPHIA, PA.

Within comparatively recent years the United States Department of Agriculture has introduced into southern horticulture two exotic vegetables—the Trinidad dasheen and the chayote.

The success attending their experimental culture and the steadily

<sup>1</sup> Read at the annual convention of the Pennsylvania Pharmaceutical Association, Buena Vista Springs, Pa., June 26, 1919.

increasing demand by the populace of many sections have encouraged their commercial cultivation to a limited degree. It may be safe to predict, however, that when the delicacy of their flavor becomes more generally known, they will be cultivated to such an extent, as to be common articles of our markets alongside of the potato and the squash.

#### THE TRINIDAD DASHEEN.

The Trinidad dasheen was introduced into the United States from the island of Trinidad, West Indies. Its native home was



FIG. 1. Trinidad Dasheen plant, *Colocasia esculenta* (L.) Schott, of three months' growth, raised in the greenhouse of the Philadelphia College of Pharmacy.  $\times \frac{1}{9}$ .

probably China, partly because the taro varieties closely allied to it have been found growing in that country and partly because its

name appears to be a corruption of the French phrase "*de la Chine*," which means "from China."<sup>2</sup>

*Description of Plant.*—The plant is a variety of the species *Colocasia esculenta* (L.) Schott, a member of the *Araceæ* family, and closely related to the common elephant ear plant of our gardens. Its underground parts (Fig. 3) consist of a large central corm



FIG. 2. Aërial portion of the Trinidad Dasheen, *Colocasia esculenta* (L.) Schott, as grown in the P. C. P. greenhouse. Note the long petioled, peltate leaves, whose laminæ show auriculate basal lobes.  $\times \frac{1}{6}$ .

weighing from two to four pounds, of spheroidal or broadly fusiform shape and reddish-brown color, and, in addition, numerous lateral cormels, which spring from various nodes along the periphery of the mother or central corm. Both mother corm and lateral cor-

<sup>2</sup> R. A. Young, "The Dasheen; its Uses and Culture," Separate 689, U. S. Dept. of Agriculture Yearbook, 1916.

C. F. Langworthy and A. D. Holmes, "The Digestibility of the Dasheen," Bulletin 612, U. S. Dept. of Agriculture, 1917.



mels are marked by the presence of numerous rings which represent leaf scars. When the lateral cormels are removed large circular to ovate light colored spots are exhibited. The total from one hill of these underground portions ranges from four to thirty pounds.

The above ground parts (Fig. 2) consist of several petiolate, auriculate, peltate, bright green leaves, three feet or more long and a spadix, which is free and terminated by a sterile appendage.

*Histology.*—When examined microscopically, sections of the Trinidad dasheen corm show the following histological peculiarities, passing from periphery toward the center.



FIG. 3. Two mother corms with their lateral cormels, the product of an 11-pound hill of Dasheens. (Photograph by R. A. Young in Separate 689 from U. S. Dept. of Agric. Yearbook, 1916.)

1. A zone of cork composed of numerous layers of cells with suberized walls, varying in shape from irregular polygonal to rectangular.

2. A broad zone of phellogen, composed of more or less rectangular shaped tangentially elongated cells with rich protoplasmic contents.

3. A broad central matrix, composed of parenchyma tissue, the cells of which are mostly thin walled and abundantly filled with starch. The starch grains are mostly simple, but compound grains composed of up to eight units are occasionally met with. The simple grains vary in outline from rounded to irregularly rounded

to irregularly ovate or angular. Some of these are devoid of striations or a distinct hilum, while others, as shown in Fig. 5, show both of these structures. In size, they range from  $3\mu$  to  $19.2\mu$ . The hilum, when distinct, varies from linear to circular, to angular or to several cleft. The lamellæ and striations, when distinct, are always concentric. These, along with the hilum, may be well ob-

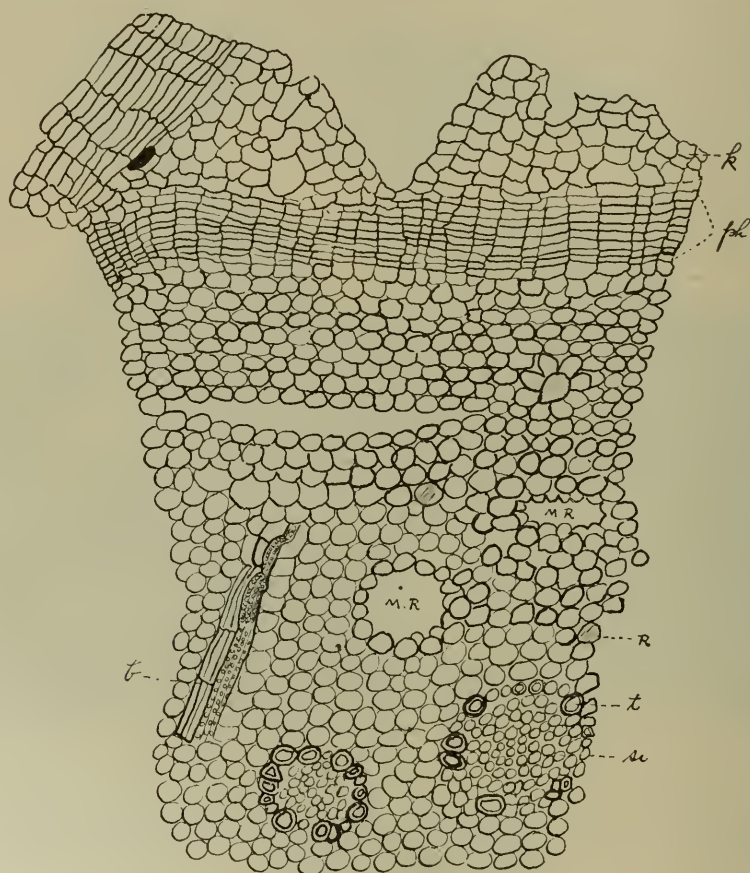


FIG. 4. Cross section of a portion of the corm of *Colocasia esculenta* (Trinidad Dasheen), cleared with potassium hydroxide solution, showing cork (*k*), phellogen (*ph*), raphides of calcium oxalate (*R*), trachea (*t*), and sieve tube (*si*) of concentric fibrovascular bundle, and longitudinal view of portion of a bundle (*b*).  $\times 18$ .

served in a mount stained with dilute gentian violet. Scattered throughout this region are to be noted numerous mucilage reservoirs of irregularly rounded, oval or ellipsoidal outline, whose contents are deeply stained with basic aniline dyes.

The fibrovascular bundles are of concentric type and may be found scattered throughout the section in irregular fashion. From

the main axis bundles numerous branch bundles emanate at various levels, which course out into the lateral cormels.

Crystals of calcium oxalate in the form of raphides are found in numerous cells of the central matrix (Fig. 4).

*Uses of the Dasheen.*—The portion of the plant suitable for diet are the corms with their lateral cormels and the aërial shoots. The former are not intended to replace the white or the sweet potato, nor the latter, the asparagus, but rather to augment the comparatively small number of starchy vegetables now in use in our country. The underground parts which are sold as “dasheens” in some of our



FIG. 5. Starch grains from parenchyma cells of the Trinidad Dasheen corm and cormels (highly magnified).

markets contain about 50 per cent. more protein and 50 per cent. more starch and sugars than the potato tuber. The average of ten analyses of these portions made by the Department of Agriculture is as follows:

	Per Cent.
Solids .....	37.235
Ash .....	1.3
Starch .....	26.097
Soluble sugar .....	1.75
Ether extract .....	.157
Crude fiber .....	.71
Proteids .....	3.03
Pentosans .....	1.24

The corms and cormels are employed in the same manner and in quite as many ways as the white potato. They may be served baked, mashed, scalloped, stuffed, cooked with grated cheese, and “French” or “German” fried. The seasoning is similar to that employed for the white potato. When baked or boiled, the interior



of a mature specimen is mealy, though firmer than the potato, because of its comparatively lower water content. Its flesh varies in color from cream to more frequently grayish white or tinged with violet.

Dasheens are best eaten directly after they have been baked or boiled. If kept standing they gradually lose in palatability.

An excellent flour has been made from dasheens. The corms and larger cormels are pared and either sliced or shredded and then dried and ground in a mill. This flour is mixed with that of wheat or rye in the proportion of one part of the former to three or four parts of the latter.

The shoots are commonly blanched by forcing them from larger corms in the dark and are said to be more tender than those of asparagus.

#### THE CHAYOTE.

This vegetable, concerning which little has been recorded, is the fruit of *Chayote edulis* Jacq. (Family Cucurbitaceæ), a native of

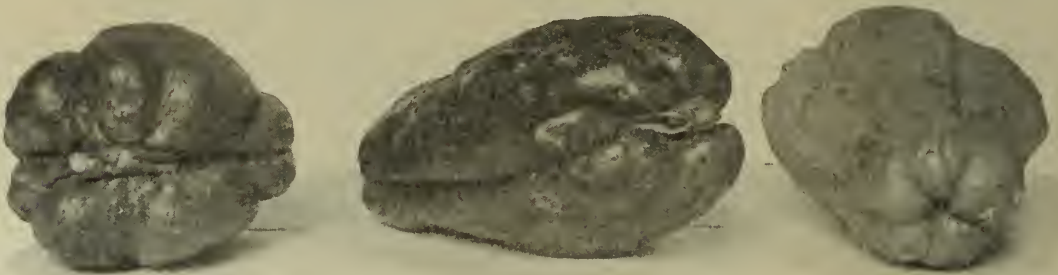


FIG. 6. Fruits of the Chayote, *Chayote edulis* Jacq. Note the embryo protruding from the distal end of each of the fruits in center and the left of the figure.  $\times \frac{1}{3}$ .

tropical American. The plant is a climbing, sparsely hairy vine, with perennial tuberous roots. Its stem bears alternate, cordate, palmately 3-lobed or angled leaves, which are membranous in texture. From points along the stem opposite the leaves 2-5-branched tendrils arise which assist the vine in climbing. The flowers are monœcious and axillary; the pistillate are solitary, while the staminate are borne in small clusters. The calyx tube is crateriform with a 5-lobed limb. The greenish to cream-colored corolla is rotate, deeply 5-parted, the segments being ovate-lanceolate. The filaments and styles are connate into a central column of which 2-celled anthers appear as lobes.

The stigmas are closely set together forming a small head. The ovary is inferior. The fruit is a greenish or ivory white, fleshy, pear shaped or globose, one seeded pepo (Fig. 6). Its surface is more or less corrugated and marked by the presence of spines around both ends. The embryo protrudes from the center of the distal end before the fruit is mature. The seed is exalbuminous and consists of a seed coat firmly adherent to the endocarp and enclosing two cotyledons, a plumule and a radicle. The cotyledons attain a length

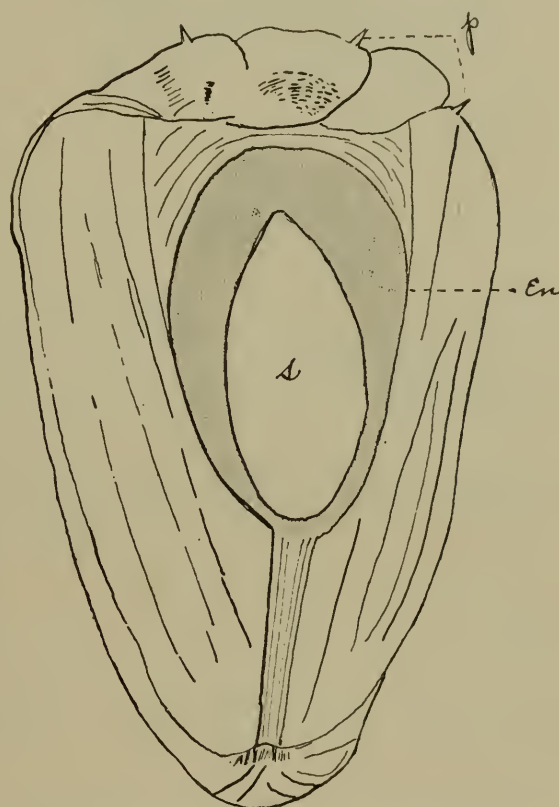


FIG. 7. Fruit of *Chayota edulis* Jacq., cut lengthwise with embryo and portion of pericarp removed. The dotted area (*en*) indicates the surface of the endocarp which is not adherent to the seed coat. Note seed coat (*s*) and spine (*p*).  $\times 1\frac{13}{20}$ .

of from 2 to  $2\frac{1}{2}$  inches, averaging one half the length of the fruit. The average weight of the fruit is about 8 ounces (Fig. 8).

According to a circular issued by the United States Department of Agriculture, the chayote may be grown successfully on any well-drained, cultivated land in sections of the Southern States where the ground does not freeze,—anywhere south of a line drawn from Charleston, S. C., to Baton Rouge, La.,—and along the Gulf coast

of Texas. It has fruited at some points north of this.<sup>3</sup> It is reported to have been grown in California.

*Histology of Fruit.*—With other cucurbitaceous fruits, that of the chayote agrees in the fusion of the receptacular to the carpellary portions during the developmental process. (

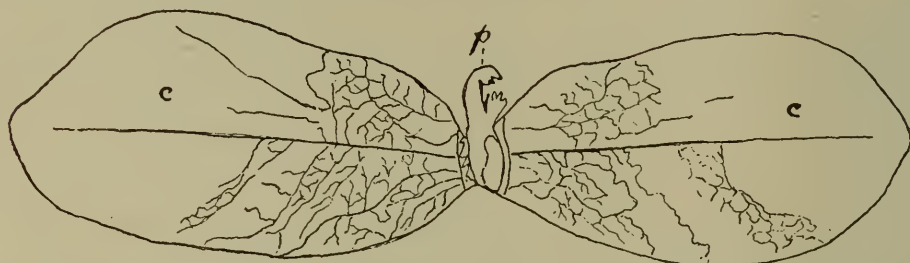


FIG. 8. Embryo of *Chayote edulis* Jacq. Note plumule (*p*) and inner surface of cotyledons (*c*) which have been spread apart.  $\times 19\frac{1}{2}$ .

*Receptacular Portion.*—This region constitutes by far the greater portion of the fruit area. In surface section (Fig. 11) the outer epidermal cells are polygonal in outline and richly protoplasmic. Many of these contain small prisms of calcium oxalate. Scattered all over



FIG. 9. Various types of starch grains found in the mesophyll cells of the Chayote cotyledons (highly magnified).

this region and interspersed among the regular epidermal cells may be noted small groups of cells, not unlike the other cells in shape, but having thicker walls and yellowish to light-brown fixed oil contents. Stomata are also found in moderate numbers in this region.

<sup>3</sup> Circulars and Pamphlets on "The Dasheen and Chayote," issued by the U. S. Dept. of Agriculture.

L. P. Byars, "A Nematode Disease of the Dasheen and its Control by Hot Water Treatment," *Phytopathology*, Vol. 7, No. 1, January, 1917.

L. L. Harter, "Storage-rots of Economic Aroids," *Jour. Agric. Research*, U. S. Dept. of Agriculture, Vol. 6, No. 15, July 10, 1916, pp. 549-572.



These with their guard cells are broadly elliptical in outline. Each is surrounded by five neighboring cells. In cross section (Fig. 10) the outer walls of the epidermal cells are slightly convex and cutinized. Beneath the outer epidermis is a zone of several layers of parenchymatous cells, many of which have lignified walls. In some instances lignification occurs in the walls of the cells directly underneath the epidermis, while in others the lignified elements are sepa-

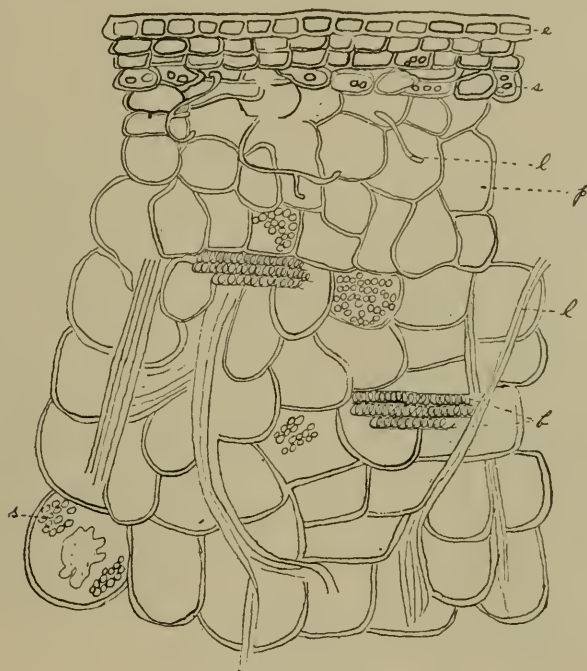


FIG. 10. Transverse section through receptacular portion of Chayote fruit showing epidermis (*e*), parenchyma (*p*), latex tubes (*l*), portion of fibrovascular bundle (*b*), and starch grains (*s*).  $\times 95$ .

rated from the epidermis by one to several layers of cells with non-lignified walls. The next broadest zone of the receptacle is composed of more or less radially elongated, thin-walled parenchyma cells, comparatively small in the outer region but gradually becoming larger toward the center. Numerous branched latex tubes, with yellowish contents, course irregularly through this region. Fibro-vascular bundles of the bi-collateral type are also to be noted. The most conspicuous elements of these are the spiral ducts which attain a breadth of 28 microns.

*Carpellary Portion.*—Separating the receptacle from the carpellary portion of the fruit may be noticed a sharply demarkated band of cells, three layers thick (Fig. 13). Of these the outer layer and

inner layer are comparatively clear, while the middle layer is filled with dense protoplasmic contents. The innermost layer of cells of this region is the broadest, contains starch grains, and doubtlessly represent the epicarp of the ripened carpellary wall.

Passing from this region toward the embryo will be noted numerous layers of thin-walled cells of rounded or irregular outline, whose lumina contain either protein or carbohydrate contents or both. This region constitutes the mesocarp. It is traversed by nu-

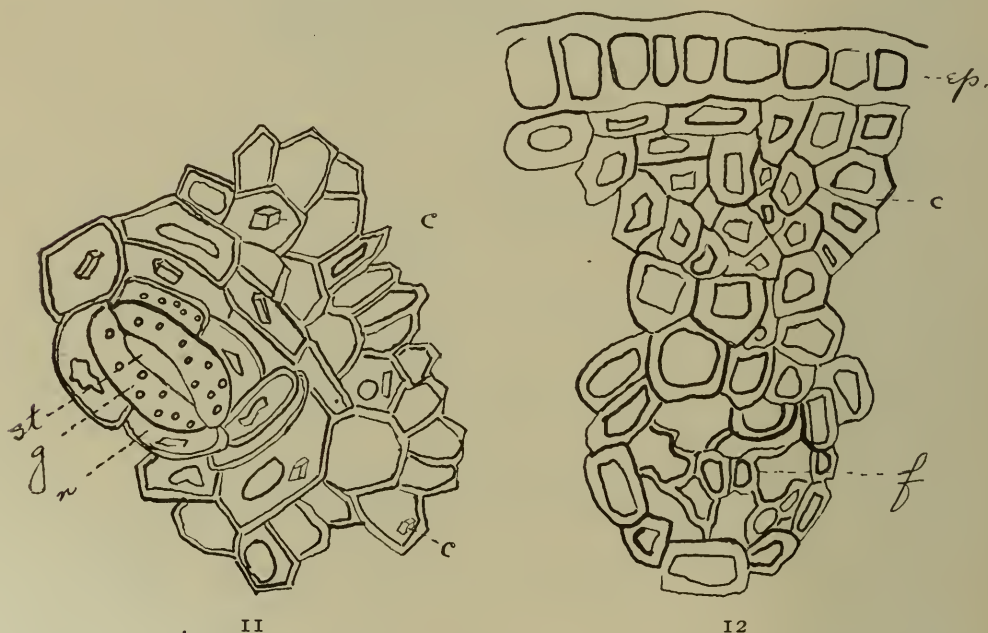


FIG. 11. Surface section of epidermis of receptacular portion of Chayote fruit. Note stoma (*st*), guard cells (*g*), neighboring cells (*n*), and crystals (*c*) within epidermal cells.  $\times 400$ .

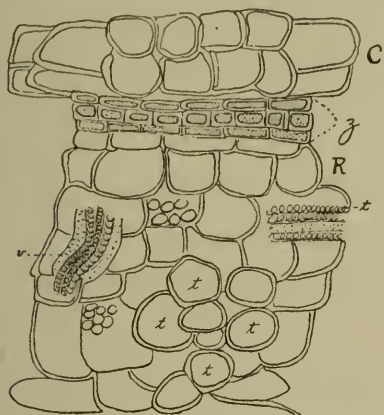
FIG. 12. Transverse section of a representative portion of a spine of Chayote fruit. Epidermis (*ep*), thick-walled cells of cortex (*c*) and vascular tissue (*f*).  $\times 75$ .

merous bi-collateral bundles. The endocarp consists of a layer of rather small tangentially elongated cells. Over that portion of this region which is unattached to the seed coat (Fig. 7), the cells are larger and have very thick brownish walls.

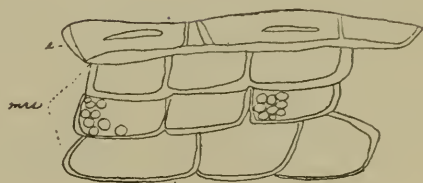
*Seed.*—The seed coat is composed of tangentially elongated cells, the outer walls of which are united firmly to a portion of the endocarp.

*Cotyledons.*—The outer covering tissue or epidermis consists of a layer of cells, which, in surface view are polygonal, and rectangu-

lar when observed in tranverse section. Many of the cells of this tissue possess starch grains. Branched stellate hairs and glandular hairs are scattered over this tissue (Fig. 15).



13



14

FIG. 13. Cross section through portion of Chayote pericarp including zone of union ( $z$ ) of receptacular ( $R$ ) with capellary ( $C$ ) portions; fibro-vascular bundle running transversely ( $v$ ), and tracheæ ( $t$ ) running longitudinally.  $\times 70$ .

FIG. 14. Transverse section of area of endocarp and mesocarp of Chayote fruit, facing that portion of the central cavity which is not occupied by seed, showing endocarp ( $e$ ), which is thicker-walled in this region than elsewhere and mesocarp ( $mes$ ).  $\times 70$ .

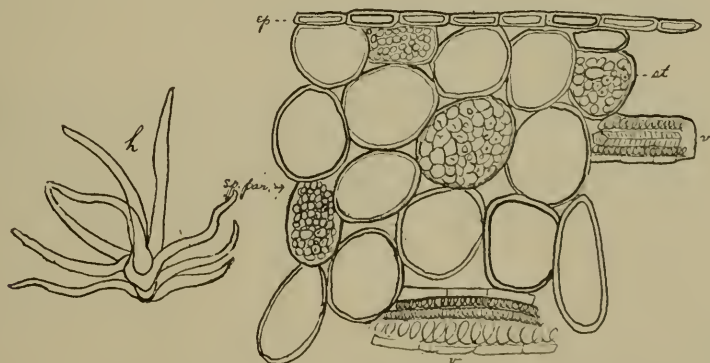


FIG. 15. To right, Transverse section of representative portion of a cotyledon of *Chayota edulis* Jacq., showing epidermis ( $ep$ ), spongy parenchyma ( $sp$ ), starch grains ( $st$ ), and veins ( $v$ ).  $\times 120$ . To left, stellate hair from epidermis of cotyledon.  $\times 90$ .

Beneath the epidermis will be noted spongy parenchyma tissue composed of somewhat spheroidal to polygonal shaped cells containing starch grains, which are mostly simple, spheroidal or plano-



convex, rarely 2-3 compound (Fig. 9). These have an average range of 3 to  $28\mu$  in diameter. Occasionally somewhat elongated ovoid-shaped grains are seen which attain a length of  $40\mu$ .

*Radicle*.—This shows the usual cucurbitaceous structures typical for that portion of the embryo. The cells of the cortex are rich in protoplasm, have prominent nuclei, but are entirely devoid of starch.

*Uses of Chayote*.—The fruits should be picked from vines when but two thirds or three fourths grown. They lose their delicate flavor and become tough, if allowed to mature. They are then cut into halves or quarters and boiled. The boiled fruit can be creamed, baked, fried, or made into fritters, sauces or salads, similar to the squash.

The vines, tuberous roots and fruits may be used as fodder for stock. The woody-stems furnish a fine fiber known to the French as "*paille de chouchon*."

BOTANICAL RESEARCH LABORATORY,  
PHILADELPHIA COLLEGE OF PHARMACY.

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## CONSTRUCTIVE SUGGESTIONS FOR THE REVISION OF THE PHARMACOPŒIA.<sup>1</sup>

BY DR. FRED. B. KILMER,  
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"Great economic and social forces flow with tidal sweep over communities only half conscious of that which is following them. Wise statesmen are those who foresee what time is thus bringing, and try to shape institutions and to mold men's thoughts and purpose in accordance with the change that is silently surrounding them."—VISCOUNT MORLEY.

We see the curtain lifted upon the tenth revision of the United States Pharmacopœia. Each decennial revision of the Pharmacopœia has marked an era, and this one perhaps more than all that have gone before. A pharmacopœia, such as ours, more than any single volume, records the progress of medicine, of pharmacy, of surgery and of allied sciences.

The ninth revision carried forward the last decades of the old

<sup>1</sup> Presented at the annual meeting of the New Jersey Pharmaceutical Association, Atlantic City, June 10, 1919.

century, in which had taken place great world changes. It was during that time that surgery moved forward a thousand years in a day. Procedures, startling in character and far-reaching in results, followed each other in quick succession.

No one has yet written the full measure of the progress in the practice of the healing art of the days just past. All this has wrought a most profound change in the practice of medicine, pharmacy and surgery, and had an important bearing upon our pharmacopœia.

The present revision comes in the dawn of a new time. Constitutions, nations, races, peoples—the whole world—has been shaken to its innermost depths. We emerge from the ravages of the world war-torn and bruised. The effects upon peoples, upon science, upon the practice of medicine and pharmacy, are not at the moment clarified, but we must take up the burden with stout hearts and a full hope.

#### SCOPE OF THE PHARMACOPŒIA.

The two last revisions of the pharmacopœia have been the basis of an unusually extended discussion as to the nature and scope of such a work. In these discussions it is quite evident that the real nature of the pharmacopœia has been lost sight of.

Charles Rice, the master maker of pharmacopœias, stated that, "at the present day the work may be considered prescriptive for, and descriptive of, medicine." He stated that the manufacture of certain classes of pharmaceutical preparations is becoming more and more concentrated in the hands of large institutions. The function of the pharmacist is chiefly confined to the examination of the preparations and substances which he buys, by means of such tests as are available to him.

Recognizing this condition, the later pharmacopœias have eliminated working processes for preparations which have passed almost entirely into the hands of the large manufacturer and have substituted for them more detailed descriptions and tests.

Under these definitions it is quite apparent that the pharmacopœia is not a text-book, either for medical, pharmaceutical, or chemical students; it is not a working manual for the manufacturer; it is not a guide for the practice of medicine, nor a code book for the collector of customs and the food and drug inspector.

## PHARMACOPŒIAL STANDARDS.

The pharmacopœia has been styled as a "book of standards." This is not its entire scope. Officially the British Pharmacopœia declares its object to be "to afford to the members of the medical profession and those engaged in the preparation of medicines, one uniform standard and guide whereby the nature and composition of substances to be used in medicines may be ascertained and determined."

The chief object of the pharmacopœia under this definition is to insure uniformity in medical substances.

According to Charles Rice, the term "standards" applied to pharmacopœial preparations, comprises three distinct features: Quantitative determination of the active principles, identification of the active principles, adjustment of strength.

He believed that standards need only be applied to drugs of importance and potency.

The convention of 1900 adopted what is known as the "purity rubric," which rubric declared the percentage of pure substances, and the limit of the inactive impurities permitted. This rubric was intended to apply to the articles contained in the pharmacopœia only when used for medicinal purposes, allowing articles used for technical purposes, or in the arts, to vary from the standard in the pharmacopœia.

The drug inspector and the customs house officer are mainly interested in the standards as defined in the pharmacopœia, and for them the more rigid and the more technical the better. The drug broker and the patent medicine man would prefer standards of maximum elasticity.

It has been urged in respect to the descriptions and standards for drugs of botanical origin, that they were too finely drawn. We may certainly contend that under the stress of war, and in the face of a scarcity, amounting almost to a famine of certain drugs, the pharmacopœial requirement that drugs must be that of a given country's origin, or in other cases could not be used because they contained too large a percentage of an unofficial portion of the same plant, or were not of the specified period of growth, our pharmacopœial standards were unnecessarily rigid.

By all means, we may at this time urge that our standards be so arranged that American grown drugs upon which so much sacrifice



and energy have been expended, shall be fostered, continued and protected.

#### THE MEDICAL MAN AND THE PHARMACOPŒIA.

The several last revisions of the pharmacopœia called forth acrimonious criticisms on the side of the medical practitioner. It should be recollected that in its inception the pharmacopœia was purely a medical document. The first edition stated on its title page that it was published by the authority of the medical societies and colleges. At the time no college of pharmacy existed in this country. The medical control continued in the three subsequent revisions.

In 1850 pharmacists were recognized as delegates to the convention, and from that time forward pharmacy took an active part in the work of revision.

The criticism of medical writers are on one hand directed against certain drugs and preparations which are contained in the pharmacopœia. On the other hand, the work is criticized because certain drugs and preparations are omitted. "You're damned if you do, and you're damned if you don't." One medical writer styles the pharmacopœia "a medical barbarism," and wants half its pages cut out.

On another side the contention has been that the pharmacopœia should contain every article used in medicine. A practitioner of medicine has stated that "if a physician prescribes brick dust, that brick dust must be defined by the pharmacopœia." Again, there are a small number of critics who are primarily pharmacologists, who intimate that "there is no use for any drug that has not been proven on frogs."

As to the great variance of medical writers on what should not be admitted to the pharmacopœia, Professor Remington tersely says, that "While it is true there are plenty of things in the pharmacopœia that the doctors in Chicago never thought of using, it is equally true that the doctors in Texas, or somewhere else, do use them largely, and the doctor there is just as much entitled to a standard for his preparations as the doctor in Chicago, or Philadelphia, or New York, who has never heard of these articles."

Physicians naturally do not take much interest in the botanical or chemical description, or in the tests for identity or for purity. According to Charles Rice, the main objects which a physician usu-

ally has for consulting a pharmacopœia are to ascertain the preparations or forms which are available in the case of certain drugs, the strength of the respective preparation, and the ordinary dose. This authority has stated likewise that the pharmacist at his prescription counter has to look for precisely the same information as the physician desires.

In one of the early editions of the pharmacopœia it was plainly stated that the pharmacopœia "did permit a description of medicines of acknowledged value, and of others of less estimation." It has likewise been truly urged that "should we introduce information on pharmacodynamics and on therapeutics, we would never reach the end. To limit the pharmacopœia to drugs of undoubted therapeutic value would offend many of the rank and file of the medical profession, wedded as some of them are to drugs of doubtful activity."

Notwithstanding such strictures we may well believe that the value of the pharmacopœia is admitted by all physicians, and from a summary of the discussions we may formulate the following:

The physician trusts that the pharmacist is acquainted with the information contained in the pharmacopœia.

The physician seeks only for information of practical application for himself.

Physicians regard the pharmacopœia as unprogressive, and not representing the advances and innovations constantly put forward by manufacturers and the medical profession, which is true.

Physicians do not look to the pharmacopœia as a guide for the value of medicaments.

The pharmacopœia does not contain all medicaments of value.

To eliminate from the pharmacopœia the drugs considered by one class of physicians as of doubtful value, would eliminate many drugs that are much used, and thus lessen the value of the pharmacopœia to the pharmacist.

No pharmacopœia, no rule, or no law can interfere with the practitioner who remains loyal to the old-fashioned drugs or lines of treatment.

#### POPULARITY OF THE PHARMACOPŒIA.

From a book-trade point of view the pharmacopœia would not be classed as among the "best sellers." Physicians have openly

stated that they have no use for it. Pharmacists have declared that it is one book they could get along without.

That the stated revisions of the pharmacopœia are not received with enthusiasm, and that the book does not attain popularity, is the consensus of opinion. It is interesting to note, however, that the fifth revision (1870) attained an unusual popularity. For years after it had become out of date, and a new revision had been made, the fifth edition was still being sold. At the present day, although four revisions have since been published, the edition of 1870 may still be found on the shelves of many pharmacists, and among the books used at the dispensing counter and in the laboratory. One reason for this unusual popularity is ascribed to the fact that this fifth revision contained processes and formulas which have not been carried to the subsequent revisions.

M. I. Wilbert expressed the belief that the popularity of the pharmacopœia depends to a great extent upon the price at which it is sold. Corroborating this view is the fact that the edition of 1870 was sold at a comparatively low price. The subsequent editions have been subjected to considerable criticism on account of their high price.

To meet this apparent condition, might it not be feasible to issue several editions of the book—for example, a full edition in the best binding for those who may desire this particular form, and an abridged edition for physicians, nurses and students, who may only desire to acquaint themselves with certain parts of the work?

Wilbert also stated that he believes that so far as possible the book should be one which, through its inherent merit, will present the sum total of our present knowledge in such a shape that it will eventually find its way into every shop where drugs and medicines are sold or prepared. It should be made indispensable to the working pharmacist as a guide and reference to his daily work; a book which he will learn to cherish on account of the information that it contains; a book that he will follow, because its formulas are simple and concise, and which without unnecessary care will give preparations that compare favorably in appearance and efficiency with any that can be produced by the manufacturing pharmacists.

The book should be good enough and cheap enough to appeal to the physician as a source of information, a necessary text-book to the student, and to the apothecary a manual and guide in his every day work.



It is the generally expressed opinion that the influence the pharmacopœia has among medical practitioners, and even among the public, in other words, its popularity, depends largely upon how far pharmacists are able to demonstrate their own ability to interpret the formulas and standards that are embodied in it. In short, the popularity of the pharmacopœia rests with the pharmacist.

I presented to this association certain suggestions as to how the druggist might help to popularize the pharmacopœia. Among the suggestions were these—

That the druggist should become the sales agent of the pharmacopœia. That if possible he should attempt to create a demand for the work.

That the pharmacist should endeavor to educate the public as to the meaning of the pharmacopœia, and its influence upon the trade in drugs and medicine.

That so far as possible he should educate his customers to realize that the goods dispensed in his store are made and dispensed according to the pharmacopœial standard.

It was suggested that the popularizing of the pharmacopœia would increase the reputation not only of the pharmacopœia itself, but of the druggist, and create a new view point for the customer, who, if he understood the real meaning of the pharmacopœia, instead of judging the value of an article by the price, would judge it by its integrity and by the statement on the label.

It was also suggested that druggists should have the letters "U. S. P." upon their labels and packages wherever the contents would permit.

That through the various journals, newspapers, circulars and otherwise, the pharmacist should announce the advent of a new pharmacopœia, and emphasize the fact that preparations from his store are made according to this standard.

It is possible that through measures of this character, instead of having a new pharmacopœia as an event to be dreaded, or to be endured, that it could be commercialized, and that the pharmacist, should he so desire, might make money out of the pharmacopœia.

We might here suggest the advisability of a publicity bureau in behalf of the pharmacopœia upon each recurring revision, and let this bureau, through the medical press, through pharmaceutical journals, through the lay press, and through every available channel, clearly express what the pharmacopœia is, and what it means to our people.

Let the slogan "The Pharmacopœia is For All" be driven home, and the pharmacopœia cannot fail to become popular.

#### CRITICISMS OF THE PHARMACOPŒIA.

The pharmacopœia is a much criticized book. In recent years immediately upon the issuance of a revision there has followed a flood of reviews and criticisms.

When analyzed, these criticisms are found for the most part to be very general. Often they are warped. They express only an individual, and at times a rather narrow, view. They are apt to be greatly lacking in directness. At times criticisms, when formulated, amount only to a proofreader's error either in spelling, punctuation, or even the transposition of a figure or the misplacement of a decimal. Criticisms of this character are prolific just after a new revision, and quickly cease.

The Revision Committee have manifested a rather extreme sensitiveness to criticism. In a book of such scope as the pharmacopœia it is easy to find something with which one may disagree. We can conceive that it would be rather superhuman to put together a book so profoundly affecting a diversity of interests and expect to escape criticism. Indeed it would be an evidence of stagnation if our pharmacopœia was to be considered as containing the last word. Every successive revision is only a step toward that absolute goal which will never be reached. When the perfect pharmacopœia shall be issued, man will no longer be man.

Constructive criticism, criticism that is earnest, that is deep, and that is honest—is helpful and is to be desired. If any fair number of workers in pharmacy and in medicine and in allied arts would formulate painstaking suggestions, it would go a long way towards the betterment and the upbuilding of the work.

In many dissertations upon the pharmacopœia, that appear just after its issuance, there is a preponderance of fault finding, of the tearing down and the ripping apart order. Very few are suggestions that build and strengthen.

Criticisms of the pharmacopœia should come before the revision, rather than after. To be helpful, they should be constructive rather than destructive. As a practical hint, we might add that it would be well for the writer of criticisms upon the pharmacopœia to put his suggestions in the exact language which the writer believes should

be used in the revision. Concise, definite suggestions, with brief reasons for the same, are what are most desired.

"Pharmacists, individually and collectively, are responsible for the shortcomings, errors, ambiguities and faults of the pharmacopœia, and they are in a position to point out to the committee on revision how and why the corrections are to be made, where and how the book itself may be improved to make it readily accessible as a knowledge on all matters pertaining to drugs and medicines as they are generally accepted and widely used in the treatment of disease."—LaWall.

#### THE LANGUAGE OF THE PHARMACOPŒIA.

Our first pharmacopœia was written in Latin text with the English translation on the opposite page. Latin was chosen for its supposed conciseness. As the language of science or culture, Latin has practically disappeared.

Strictures have been made against our pharmacopœia in respect to its language, its spelling, its form, its diction and its grammar. These have mainly come from a superficial review of the book. The revisers have, with care, preserved the "form of sound words" that have come down from the ages. The pharmacopœia is written in good English. The revisers have been cautious of innovations; they have made changes when such changes would tend towards force, lucidity, uniformity, simplicity and an economy of expression.

In a way the United States Pharmacopœia follows no model. It is not an essay, nor a text-book; it is neither a commentary nor a dictionary. It is a pharmacopœia—following a style and a form which it has created for itself.

In any discussion as to the language used in the pharmacopœia, we must ever have in mind what it is. Professor Remington stated tersely that "the pharmacopœia is for all." Savants, scientists, physicians, pharmacists, clerks, students, nurses; the government officials, the attorney, the judge and the jury in the court, even the man in the street, will at one time or another have cause to read the pharmacopœia. Its language must be that which will always carry the same meaning.

The fact that our pharmacopœia is written in the English language is important. We are in the beginning of a new time. As a result of the world carnage, space boundaries and racial differences



have to a marked degree disappeared. The press, the telegraph, the telephone and the phonograph have commingled and intermingled speech.

Out of this we find at most two languages which seem to have attained the balance of power, viz.: English and French. The smaller languages survive as speech, but not as the language of literature or science.

The war has put an end to the spread of the German language, or of German influence in science. Before the war the Germans themselves realized the inadequacy of their language as a world tongue. To prevent the growing predominance of English and French, the Germans invented and fostered artificial tongues, such as Esperanto.

With the coming of peace, Germany takes rank as the Ishmael among nations. Against the spread of the German tongue, German "kulture" and German science, are hostile frontiers. The nations of the earth have set their hearts, their bodies and their guns against any Germanic advance.

It foreshadows much that at the Peace Conferences the scores of nations represented conducted their sessions and wrote their documents in the English and French tongues. The French speech is smooth, light, flowing and expressive. A book in any language is easily translatable into French. The English and French languages have technical and scientific phrases which have meanings in common. Through language alone French science must hold a high place in the world's literature.

English is the language of commerce. It is predicted that it will be the world language of the future, with French as a second choice. Pharmaceutical literature in English has already encompassed the earth.

The British Pharmacopœia of 1914 was an imperial pharmacopœia, legalized and accepted throughout the whole British Empire.

The preëminence of the United States Pharmacopœia is acknowledged. American dispensatories, and such works as Remington's Pharmacy, have no counterpart in any language. It was a German, not an American, who proclaimed American Pharmacy as "the best in the world."

Through combined British and American influence the pharmacy of the world, so far as literature and practice are concerned, will, for generations to come, be under the domination of the English language.

The eighth revision of our pharmacopœia was translated into Spanish to meet the needs of Latin America. It might be suggested that the coming revision should be translated into French. This would make the work available throughout the continent of Europe where, for years to come, conditions will preclude the issuance of pharmacopœias or pharmaceutical literature.

The United States Pharmacopœia, in English and in French, coupled with the far-reaching British Pharmacopœia, must certainly dominate the world of pharmaceutical thought.

#### FUNDAMENTAL PRINCIPLES.

There are certain fundamental principles which should govern the revision and the use of the pharmacopœia. These should be kept ever in view. The whole of the vast machinery which has to do with the preparation and dispensing of medicines, must have for its foundation the pharmacopœia. The well-being of the people in sickness, in life, in death, is linked with the pharmacopœia.

One of the primary objects of the pharmacopœia is to secure the uniformity and the integrity of medicine. Without a pharmacopœia there would be medical chaos. Abolish the pharmacopœia and we are without chart, compass or rudder.

We can hardly imagine the helplessness of a people with such a preparation as the tincture of opium put out under a different standard by each dispenser.

To secure uniformity and integrity was one of the principles which governed the founders of the pharmacopœia. This vital principle existed long before the coming of the Pure Food and Drugs Law, which enactment made it into a legal standard. It always has been, and always must be, the standard else it loses its vital spirit.

The pharmacopœia is now controlled, revised and made upon the same basis as is the government of the people which it serves. A representative body makes and revises the pharmacopœia. The present makeup of this body is that which has grown with the years. Representatives from the medical profession, from associations, colleges and institutions, from certain branches of the government; representatives elected from every branch of the art and trade in drugs and medicines, control and formulate the revision.

Were the pharmacopœia to be issued under government control, or under the control of one body, of some one school or college of

medicine or pharmacy, some one organization of trade, the vital breath would disappear.

The pharmacopœia must be representative—it must not be formulated for one school of medicine to the exclusion of another, for one state or one locality to the exclusion of others. It must not be a college text-book, or a manufacturer's compendium. It must not tear down or build up one branch of pharmacy or of medicine. It is not a book of regulations for the use of bureaucratic inspectors. Its foundation must be broad, wide, deep—for the people of the realm whose representatives founded and kept it where it is.

The authority for the pharmacopœial revision should not be vested in one man or even one set of men. We must maintain a system of checks and balances. The authority and the responsibility must be divided. We are told that concentration would make for efficiency. On the other hand, concentration would also make for tyranny.

Put the making of the pharmacopœia in the hands of a drug inspector, and it would emerge a set of rigid standards and tests, covering a most restricted number of substances. Put the revision in the hands of a physician and he would select a dozen drugs, and enact that these drugs and no others were to be recognized for use in medicine.

While the ever-increasing complexity of the problems involved in revising the pharmacopœia, demand that for efficiency there must be a concentration of power as well as a division of labors, we must ever guard against the concentration of power into one school, one party, or one man.

It is vital that the fundamental principles of the pharmacopœia shall be known and accepted by all who have to do with that which is written between its covers. This means that those who in any way have to do with the making, handling, selling, buying or dispensing of medicines must support the pharmacopœia. It is the pharmacopœia of the people, for the people and by the people. The breath of this life, its continued vitality, depend upon the general and intelligent acceptance of it by all people. Pharmacists, chemists, druggists, physicians and patients alike must have faith in it, must believe in it, must uphold it.

The pharmacopœia is far from complete. It is for this reason that provision has been made for its periodic revision. But there are certain underlying principles which cannot be destroyed or im-



paired without wrecking the pharmacopœia. There exist certain forces which tend to undermine and subvert these principles. These forces must be checked. All true pharmacists, all true physicians, all true Americans should cry "Save the Pharmacopœia."

While antagonism to the principles of the pharmacopœia is serious, ignorance and indifference towards it is of a graver aspect. Too many medical men administer medicines without a knowledge of, or without regard to the pharmacopœia. It is seldom a living part of the practitioner's armamentarium. Buyers and sellers of medicine only respect it to the extent that they may keep "within the law." In drug stores it has been stated that they could get along without it. The college student may "cram" up on the definitions of the pharmacopœia, but he has no real knowledge or care as to its philosophy, or the principles which underlie and make it what it is.

Whatever else the graduate in pharmacy may know, he should not receive a degree until he can show a knowledge of the history and fundamental principles of the pharmacopœia. In all departments of life we find that at this time there is a revolt, a hostility against that which has the sanction of the past. There is a craze for innovations.

In this struggle the pharmacopœia should steadfastly be maintained, true to its traditions, true to its principles. The pharmacopœia is the hope of pharmacy, the hope of medicine—let it be ours to see that it does not perish.

#### THE SPIRIT OF REVISION.

The direct charge has been made that the pharmacopœia has become commercialized, that the dominant influence has been that of the manufacturer and the purveyor of medicines. The oft-repeated statement that pharmacy has become commercialized is a statement of fact, and it may be stated likewise with truth that medicine has become commercialized.

In these days, costs, expenses, incomes, profits are before us with increasing intensity.

Whatever a man may wish to do it is a preliminary consideration that his achievements must have a money value. No matter how gifted he may be, he must turn his powers into coin or he cannot use them. We live in a day where the getting and keeping of money is the superior gift to which all others must bow.

Through pharmacy the spirit of gain has, in some measures, run like a choking weed. The same condition is apparent in the status of the medical profession. Nowadays a doctor is simply one of the many engaged in the fierce struggle for existence, in the race for wealth. It is not to be inferred that much good has not been achieved in the struggle for gain. We cannot deny the achievement of commercial pharmacy, of commercial chemistry, nor should we detract one jot from the wonderful achievements of the worthy specialists in medicine and surgery.

The point to be urged is that where the gain and profit is to subordinate all other ends, our work is crippled. In approaching such a task as the revision of the pharmacopœia, we must hope that the spirit of gain which rules our lives will emerge as a spirit of service.

Gain in one branch of the trade as against another, gain in one class of medicine or pharmacy over another class, the preëminence of any college, school or clique must be made to disappear.

While recognizing the commercial conditions which surround the making, selling and administration of medicine, we must approach our task seriously in the spirit of service. The mission of the pharmacopœia is to serve the art of healing, to serve mankind. The ultimate end to which the application of the pharmacopœia is designed is that of the suffering patient. In pharmacy and in medicine more than in any other art in making a thing a better thing or an old thing in a better way, we are doing a good that shall never pass away.

The recognition of the spirit of service above the spirit of gain in the revision of the pharmacopœia is full of promise. It is with this spirit we must look to its uplift, its moving forward and its permanency.

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## MAKING MONEY OUT OF "BUGS," BY USING INFORMATION FROM "UNCLE SAM."<sup>1</sup>

BY GEORGE M. BERINGER, JR., P.D.

CAMDEN, N. J.

"Mister! Gimme sumthin good for bedbugs. They nearly et my little Jimmy up last night," or "Can't you recommend something for roaches? I don't have any, but my next-door neighbor is house-cleaning and they are coming to me in droves."

<sup>1</sup> Read before the New Jersey Pharmaceutical Association at its annual session, June, 1919.

Such are the complaints with which the druggist is continually having to deal. Often, I fear, his answers are based upon popular ideas that have but little or no scientific value and which are, in many cases, absolutely worthless. The subject is one which is important enough for a more careful consideration. The pharmacist who knows what he is talking about, in the matter of insecticides, can surely build up a trade in that line which will give him handsome returns. He can acquire the necessary information with little effort and practically no cost. "Uncle Sam" will furnish it through the Department of Agriculture.<sup>2</sup>

Every live pharmacist should have his name on the list of the Department of Agriculture to receive its monthly list of publications. For the price of a post card, he can have information regarding not only insecticides, but also regarding diseases of plants, cattle, domestic fowl and the remedies for such diseases, and regarding drug plants, wild and cultivated, and a host of other subjects of which he never dreamed. The man with a country store would, of course, profit most largely by this information. I have noticed, however, that when a countryman drops into the store of a city druggist for something not kept by his rural confrère, his interest is very easily gained if the city man can show him that he is interested in the problems that concern him and can intelligently offer suggestions. A country customer, so won, advertises such a store to his neighbors, and soon there is built up a clientele that could be had in no other way.

The use of insecticides, as usually considered, may be grouped under two heads, for the destruction of household vermin and for the destruction of insects infesting plants. This paper will be confined to the consideration of such insecticides as are used for the destruction of household vermin. In this part of the country there are but three kinds of insects which give much trouble in the household—bedbugs, roaches and moths.

When used against bedbugs:

Hydrocarbon oils, as gasoline and kerosene, and preparations consisting largely of the same, are 100 per cent. efficient.<sup>3</sup>

Kerosene proves the better by reason of the fact that it

<sup>2</sup> This paper is based upon Bulletins Nos. 701 and 771 of the Department of Agriculture, together with a few observations of the writer.

<sup>3</sup> Wherever "efficient" is used in this paper, it is to be understood to mean that such a percentage of the insects used in a test were destroyed.



destroys the vitality of the eggs, gasoline being less efficient, apparently because of its greater volatility.

Coal-tar-cresote emulsions, *i. e.*, preparations of the type of creolin, are 100 per cent. effective when used undiluted, but are not very valuable when diluted, as they must be in practical application.

Mercuric chloride, in 6 per cent. solution and in powder, is 100 per cent. effective. It is too poisonous, especially in the powder form, for promiscuous use.

Pyrethrum powder is very effective. If the powder contains much stem, it is worthless.

Turpentine oil is 100 per cent. effective.

Sabadilla seed in powder is 100 per cent. effective. This is often used for destroying body lice, but is not generally known to have value in destroying bedbugs.

Sulphur, when burned, under proper conditions, at the rate of one pound to a thousand cubic feet of space, is effective against both bugs and eggs.

Among substances popularly supposed to be of value, but which tests prove to be worthless or nearly so, are:

Paraformaldehyde, even when used in the proportion of two and one quarter pounds to one thousand cubic feet of space.

Formaldehyde, diluted 1-14 and used as a spray.

Sodium fluoride.

Paris Green.

When used against roaches:

Sodium fluoride is 100 per cent. effective, and, even diluted with inert powders to 18 per cent. strength, is still very effective.

Hydrocarbon oils, as gasoline and kerosene, and preparations consisting largely of the same, are effective if they come in contact with the insect. Roaches, however, are not obliging enough to come out of hiding in any considerable numbers except at night and when left alone. For this reason, the use of such substances is in the same category as catching a bird by putting salt on its tail.

Among substances popularly supposed to be effective, but which tests failed to prove as efficient as the above are:

Borax, partially effective, but slow.

Phosphorus pastes, partially effective, but slow.

When used against moths:

Naphthalene is very effective in killing adult moths, larvæ and eggs.

Camphor is very effective, but less so than naphthalene.

Cedar chests prove to have power to kill adult moths and young larvæ.

Cedar chips give some protection, but are not entirely effective.

Cedar leaf oil is very effective.

Pyrethrum powder is 100 per cent. effective on larvæ and is an excellent protective.

Kerosene and gasoline are effective, gasoline, in particular, killing the eggs.

Strong soap suds will kill larvæ and eggs on flannel.

Sulphur, when burned, is partially effective.

Heat, in an oven, at 110° F. for 31 minutes is effective.

Hot water at 140° F. for 10 seconds is very effective.

Powdered cloves appear to have considerable value.

Among substances generally supposed to have value, but proving ineffective in tests are:

Lavender flowers, though the oil of Lavender flowers has some value as a protective.

Of all the commonly used household insecticides, pyrethrum powder has, probably, the widest range of effective application. It would be more popular than it is, were it not that many facts regarding its use, preparation and storage are not well understood. To be effective, pyrethrum must be in a very fine powder. Contrary to general belief, it acts as a contact poison and it is not necessary for it to be eaten by the insect. Supposedly, it gets into the insect system through minute breathing pores along the sides of the body. For this reason, the more dust made in the air, when applying it, the better the result. It does not kill the insect immediately, but does produce a sort of paralysis at once. Death is none the less certain, however. Stems, no matter how finely powdered, are worthless. Flowers collected with long stems are sure to produce a very inferior powder if the stems are ground with them. The same is true, of course, if stems are added during or after grinding.

Pyrethrum, in powder at least, does not retain its strength indefinitely. Both whole flower heads and powdered have been found to retain their activity for about three years. Powdered flowers

have been found to have lost their activity when kept for five and one half years. The powder should be kept in tightly closed containers, as the powdered flowers, exposed to the atmosphere in a room for 136 weeks, were found to have lost considerable of their value. Exposure to weather for 21 weeks also greatly reduced their efficiency. High temperatures have been found to be deleterious.

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## PHARMACY AND PUBLICITY.<sup>1</sup>

BY E. G. EBERLE, PH.M.,  
PHILADELPHIA, PA.

No one doubts that publicity has educational value and shapes public opinion. Advertisements conveying messages impress the minds of individuals, editorials shape the thoughts of citizens, and important and sensational news items interest the readers. The importance of publicity as an influential factor in shaping public opinion can hardly be overestimated.

The lasting impression or effect of publicity depends upon the value of that to which publicity is given in the affairs of men and nations, and the accuracy or truthfulness of the statements. But no matter how untruthful the latter may be, the average citizen does not investigate but accepts as truth that which appears in print. Whether right or wrong, the public estimate of occurrences, of aims and purposes, of government, business and professions, does not always conform to facts. The absence of proper conception or exact knowledge leads to acts which do injury and develop a prejudiced estimate.

Druggists are engaged in a semi-professional business which has many ramifications and its activities come into contact with trades and professions. The former use methods of competition, while the latter, not infrequently, hold themselves aloof from the more intimate relations which should exist.

Not only the complexity of the drug business, but the fact that the dispensing of medicines must be regulated, stimulates national and state legislators' legislative propensities. The enacted laws are not infrequently framed on erroneous views or misinformation.

<sup>1</sup> Read at the annual meeting of the Pennsylvania Pharmaceutical Association, 1919.



The few points made could be multiplied, but are simply intended to emphasize the necessity for publicity on the part of pharmacists,—publicity which is truthful and will lead to a better understanding by the public of pharmacy and the drug business, also to direct attention to the need of correcting misstatements which so often go unchallenged and hence are accepted by the laity as truths. The fact that pharmacists were practically ignored in the Service was largely due to deficient publicity. The multiplex federal taxation, the methods of regulations applying to revenue laws concerned with narcotics and alcohol are in a degree tinged by misunderstanding and deficient knowledge on the part of legislators.

Along these lines Chairman H. V. Army, of the Committee on Federation A. Ph. A., states in Bulletin No. 3:

“We have talked a great deal about the remarkable influence of the American Medical Association, and on analysis we find that the cause of its power is publicity. We have wondered at the remarkable achievement of the American Chemical Society in developing public opinion to the extent of establishing a chemical corps in the Army, and when we seek the main factor of success we find publicity.

“We pharmacists ask ourselves why the Edmonds’ bill does not pass; why the will of one man in the Medical Corps thwarts the efforts of thousands of pharmacists; why the chemical corps gets credit for pharmaceutical work done by a pharmacist in the corps, and our answer is lack of publicity.

“A federated committee with funds sufficient to conduct the work of furnishing the daily press with news items relating to pharmaceutical progress is essential if American pharmacy is to come into its own, and the creation of such a committee would be the most practical step toward the federation of pharmaceutical bodies.”

Preparation for such coördinated and coöperative work takes time, but pharmacists and state associations can at once do a great deal in improving conditions and correcting false statements which are given out as truthful information. The assertion that pharmacists were not adequately prepared by education and training for services rendered by their fraters in continental armies has been a large contributory cause for non-recognition of pharmaceutical service, notwithstanding the fact that absolutely unqualified men were in some instances assigned duties wherein pharmaceutical education and training were necessary. Unfortunately the medical men

did not enthusiastically help in correcting these conditions, and it is this indifference which tends to retard the advance of pharmacy so essential for the advancement of medicine. When an unprejudiced analysis is made of existing conditions in pharmacy, and medicine also, for that matter, it will be found that the aloofness of the medical profession is a contributory cause. The people have a right to demand a service from the coöperative endeavor of medicine and pharmacy. These professions have been granted special privileges because they serve the public, and the latter has a right to expect and investigate their coöperation. There is a widening field of medical science before us, developed by the experiences of the world war. There should be helpful publicity, coördination and coöperation of all engaged in the activities concerned with medicine.

Statements of officials and of the press that are derogatory to pharmacy too frequently go unchallenged. The advertisements of manufacturers sometimes cast aspersions on the drug trade, and then these same manufacturers, in language that does not evidence sincerity, seek the coöperation of the drug trade. Such two-faced methods should be exposed. Without regard for actual facts assertions are made relative to methods employed in drug stores, instances of violation are given general application, but seldom is a corrected statement accorded the same publicity as that of the sensational item. The deplorable acts of an individual who is an out-cast as far as pharmacy is concerned are made the thundering charges against all engaged in pharmacy. This should not be so; publicity is needed.

And now with the general prohibition of the sale of alcoholics, druggists will have a serious condition to meet which will require their most careful thought, sincere patriotism and loyalty to the profession of pharmacy. They, unfortunately, will practically alone have the right to dispense alcoholic beverages, as medicine, and every device and scheme known to the ingenuity of man will be tried in tempting their strict adherence to their obligations. The majority will stand the test; some will fall, and then a general application of violation of trust will be made. Preparations must be made to meet the exigency rightly, or pharmacy will seriously suffer. In this, as in the sale of narcotics, conscienceless physicians will join in order to profit. It is time physicians and pharmacists and their associations coöperate to correct these despicable methods of traffic. A more intimate acquaintance will prove that the sincere in both professions desire to serve honorably and well.

This paper was hurriedly written in order to fulfil a promise, but the writer believes it conveys a message which the members of the association can discuss with profit to themselves, the association, and pharmacists generally.

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## COÖPERATION AS WELL AS ORGANIZATION.<sup>1</sup>

BY J. W. ENGLAND, PH.M.,

PHILADELPHIA, PA.

What is most needed to-day in American pharmacy is unity of effort—not only better national organization, not only better state organization, but also better national and state coöperation.

The state bodies can and do take care of state interests, and successfully, but there are many questions of state interest that are of national importance, and many of national importance that are of state interest. In other words, the interests of each are the interests of both; they are interdependent.

The wonderful success of the American Medical Association as the spokesman of American Medicine has been due to its recognition of the vital importance of national and state affiliation, and to its campaigns of publicity, both professionally and to the general public; and American pharmacy may well profit by its example.

The mainspring of pharmacy is the profession of pharmacy. Eliminate this from the drug store and it becomes a drugless drug store.

During the past fifty years, the American drug store has undergone a radical change, and rightly or wrongly, commercial pharmacy has become its dominant feature.

But there are two kinds of commercial pharmacy—a legitimate kind which consists in the buying and selling of drugs and such side lines as reasonably relate to pharmacy, and an illegitimate kind which consists in the buying and selling of almost any class of merchandise that brings money into the till, the pharmacy end of the business being simply incidental.

It is this trend toward illegitimate commercial pharmacy—towards commercialism, pure and simple—that is rapidly becoming

<sup>1</sup> Presented at annual meeting of Pennsylvania Pharmaceutical Association, June, 1919.



a menace to the existence of drug stores. There is a real public need for legitimate commercial pharmacy; in fact, the service of the American drug store in this respect is of the greatest public convenience, but this is a far cry from the illegitimate commercialism that is masquerading in the name of pharmacy, and which is injuring the professional character and standing of retail drug stores with the American public, particularly with the medical profession.

It is hardly worth while discussing the responsibility for this condition. It is here and the problem is how best to meet it. But it may be said in passing that the medical profession is primarily responsible because it has been indifferent to the profession of pharmacy *as a profession*, failing to give it that support and coöperation that was essential for its proper functioning, ignoring the fact that there is a very vital relationship between therapeutics and pharmacy and what affects one will affect the other. The responsibility is due, also, to the economic conditions that have forced retail druggists to depend more and more upon commercialism to eke out a livelihood.

The solution of such a problem—the betterment of the conditions of pharmaceutical practice—is not a state problem merely, it is one that is of interest to the retail druggists of the whole country, and the way to solve it successfully is by state and national coöperation.

There are many other questions of like import. We need, for example, better relations with the medical profession. We want physicians to recognize the importance and usefulness of pharmacy to medicine. We don't want tolerance, but we do want and need the sympathetic support and coöperation of the medical profession with the profession of pharmacy, and the way to get this is by affiliation of the state associations with the American Pharmaceutical Association, which stands preëminently for professional pharmacy, and by the latter with medical organizations.

There are many ways in which such coöperation could be made mutually helpful. For example, there is needed to-day, in the cities and towns of the country, laboratory technicians—experts in bacteriology, biology, radiography, microscopy, clinical chemistry, etc. Pharmacists could readily train as such and be of real service to the medical profession in helping to confirm or solve problems of diagnosis. But such a service would not be used unless it had the endorsement of the medical profession.

Furthermore, the problem of compulsory health insurance legislation, national and state, is looming large on the political horizon,

and unless pharmacists and physicians work together for the protection of medicine and pharmacy both will suffer seriously.

The subject of closer affiliation between the state pharmaceutical associations and the American Pharmaceutical Association should have the fullest and freest consideration from every angle. There should be no hasty action. But it does seem to me that the possibilities of closer affiliation are so obvious that it would be entirely safe, first, for every state pharmaceutical association to approve the general principle of closer affiliation, and second, to appoint the three delegates from the state association (who will represent it in the House of Delegates of the American Pharmaceutical Association) as a Committee on Ways and Means to consider the question fully and report their findings and recommendations at next year's meetings of the state associations; and, if in order, I would suggest such an action by the Pennsylvania Pharmaceutical Association.

The following resolution was unanimously adopted:

"That the Pennsylvania Pharmaceutical Association reapprove the general principle of federation as promulgated by the American Pharmaceutical Association, that we appoint our three delegates to attend the annual convention at New York in August, 1919, and instruct these delegates to state to the convention that the plan of combining the dues (American Pharmaceutical Association and state pharmaceutical associations) on the basis of 100 per cent. membership is not feasible, but that if some feasible plan can be devised for combining the dues and giving State members the publications of the American Pharmaceutical Association, we would approve of the plan."

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## COMMERCIAL ETHICS.<sup>1</sup>

BY BURWELL S. CUTLER,

DIRECTOR OF THE BUREAU OF FOREIGN AND DOMESTIC COMMERCE.

It has ever been true that no community of action can be brought about between two or more men without a community of interest. In the absence of an incentive truly mutual, even if not mutually equal, coöperation lags and active relationship between the two parties dies out.

Commerce, defined as an exchange of values, does not eventuate between two traders when one of them can find no value for himself.

<sup>1</sup> An address delivered before the Pan American Commercial Conference, Washington, D. C., June 4, 1919. Reprinted from Commerce Reports.

in the transaction. Or having chanced a trade in the hope of finding profit and then being disappointed, he will not continue to trade in that particular direction. Repeat indentures, whether between individuals or between nations, depend wholly and exclusively upon an equity of satisfaction continuously felt and frankly acknowledged.

Although this is so obvious as to be almost trite, yet we must be ever and always reminded of it when we discuss our commercial relations with other nations of the great Pan-American Union, because traders north and south are likely to be thinking of orders only, the passage of merchandise in volume, and not the spirit which creates the trade.

COMMERCIAL TRICKERY BAD SALESMANSHIP—REPEAT ORDERS  
ESSENTIAL TO SUCCESS.

There is a belief among the cynical ones of commerce that the hungry buyer will favor with his orders any business house or nation which quotes low prices regardless of the seller's lack of known reliability. I have heard it said that in the Far East, particularly, only commercial speculators, adventurers, or pirates can do business, because they expect to capture from each buyer one order only and are willing to quote any low price on any set of specifications desired, knowing perfectly that their goods are inferior and will be a disappointment on arrival; in other words, it is the policy of commercial trickery. The cynic who thinks such methods are necessary in any part of the world, simply because its people want inexpensive goods, is not only an ignorant economist but totally deficient in salesmanship. As for his morality, he might just as well propose to commit perjury in a court of law; one lie is as bad as the other.

But, of course, we are to think primarily of the well-established business man or his concern whose object is to build up and maintain a continuously agreeable and profitable trade. He knows instinctively that he must have a satisfied customer all of the time. The initial expense of finding the reliable customer, whether he be buyer or seller, frequently adds so much to the overhead cost of the first transaction that no profit remains, and yet he has foreseen this and is prepared to accept it in favor of repeat business free from contingency. Sometimes adverse conditions govern for a long preliminary period; for instance, the financial state of a foreign coun-



try may make the opening of trade depend on financial aid to the buyer, either in the form of loans or merchandise consignments, for a year or more, and this concession takes at least 6 per cent. bodily out of the profits. And our far-sighted merchant consents when able, because he is building up successful trade relations, and is not scheming for one or two profitable orders; he is not making a raid on the market; he is disposing of his output in the years to come.

OVERSTOCKING OF CUSTOMERS OBJECTIONABLE—REPUTABLE  
HOUSES SHOULD HAVE PREFERENCE.

In the organization of their sales forces the largest and best concerns of the United States—and this is equally true of like concerns in South America—do not demand of new commercial travelers a great sheaf of orders on their first trips, regardless of consequences; what they do require is a showing on subsequent trips, a constantly growing clientele on the firm ground of satisfaction and confidence. Indeed, I have known salesmen to be summarily dismissed by such concerns for persistently overstocking customers on big orders regular in every way but too forcefully stimulated.

In brief, the responsible concerns of North and South America on whom we depend for Pan-American solidarity, practice a far-sighted system of foreign trading designed for a term of years and predicated on the smiling satisfaction of their customers; speculative order taking has no place in their program.

It must also be said that our South American brothers should prefer their trade relations with North American houses of established high repute, if they want the certainty of fair treatment. For those concerns only are the ones which know they must protect their investment and their good will by judicious settlement of such errors of practice and misunderstanding as may inadvertently occur. It is the experience of the Bureau of Foreign and Domestic Commerce, in its rôle as volunteer mediator of Pan-American trade disputes, that representative North American houses are zealously eager to make the amende honorable every time. On the other hand, irresponsible commercial pirates regard any deal as closed after they have secured their money and they avoid adjudication as a burglar does a police court.

There is no such thing as a superabundance of information about any man or his concern when we are dealing with him for the first

time. Nor will he refuse to report his whole background and history unless he has something to conceal. I wish that the habit of commercial confession, on which North American domestic credits are based, might be emulated in Latin American countries instead of it being so often thought a species of impertinent familiarity.

Of course, there is no morality involved in a transaction when two traders meet each other fortuitously for the secret purpose of tricking each other. When the victim of "horse trading" cries out that the animal he received for his spavined horse was even more spavined and also foundered, the Bureau of Foreign and Domestic Commerce as mediator retires from the paddock with a smile of serene detachment. The Pan-American deserves just what he gets and nothing else.

#### BODIES FOR ARBITRATION OF TRADE COMPLAINTS.

This leads to mention of the splendid machinery for arbitration of trade complaints set up between the Chamber of Commerce of the United States and the Bolsa Commercial of Buenos Aires. It is a model that should be adopted by every South American country through its leading organizations, for, as I understand it, it provides first for helpful suggestion to the parties in the case, then mediation by locally selected judges, and, finally, in the event of intractability, for judgment in favor of the injured party if one appears. The Bureau of Foreign and Domestic Commerce expects to deliver to this impartial tribunal all complaints that defy friendly mediation after they come to us.

Please do not for even a moment infer from this discussion that we find Pan-American trade relations greatly beset with complaints or difficulties of understanding. As a matter of fact, the course of this trade for several years back, even during troublous war conditions, has been singularly free of conflict. Instead of disputes there has been a constantly augmented flow of warm commercial sympathy and admiration. The official correspondence of the United States Department of Commerce with South America frequently reads like the billet doux of a successful courtship.

#### NEED OF COMMERCIAL CREED.

But now that we have learned one another's ways and viewpoints, what common tenet of commercial faith may be found, what

creed of ethical value to which all our business interests may adhere? It seems to me that we ought to have a standard, a touchstone by which our mutual trade conduct is measured and guided. The home, the church, and the state acknowledge, each for itself, a platform of moral declaration by which it appeals for support to the peoples of the world. In different lands the articles of faith vary, but they never deviate from the supreme purpose of inculcating a common morality in accordance with the best thought of the land. The great institution which we call business deserves such a creed, so that men north and south may acknowledge it, just as most of us acknowledge allegiance to the Ten Commandments of Moses, a creed to which the guardians of economic integrity—and every honest business man is such a guardian—to which he may point and say, "You may count upon me to follow that ideal so far as it is humanly possible." It would then be possible for us to hold up any phase of business conduct to the creed and to determine how far it followed the ideal or departed from it. It would mean that in the very beginning of a transaction the several parties involved would accept the guiding principles in which they could concur without debate and thereby clear the ground of any basic misunderstanding before actual trade ensued. It would mean the same unity of spirit and purpose that actuates all the members of a church or of a political party. It would satisfy the intense longing of the honest and capable business men within the realm of the Pan-American Union to know each other better so that coördinated business conduct is made easy and pleasant.

Needless to say, the adoption of such a creed would automatically exclude from our confidence those individuals who could not or would not subscribe to its articles.

Without doubt there exists in the minds of most good business men a list of non-ethical practices which are known to commerce but are abominated. These frequently take the form of prohibitions expressed in negative terms, such as a resolution that we will not attempt to ruin another man's market by the process of selling goods below cost next door to our competitor's best customer for the sole purpose of annihilating that competitor and his customer at any cost. Likewise, no good management will throw a hard-pressed dealer into bankruptcy for the purpose of stealing his business. Neither will a good management secretly bribe a customer's purchasing agent to take goods of inferior quality at high prices. No



good management should deliberately hire away the valuable employees of another concern for the purpose of crippling it; this is an evil which is too prevalent now and would be abolished if there could be an agreement on its unmoral character. No good management thinks it permissible to adulterate the goods of a competitor and then to sell as of representative value in order to damn the competitor in the eyes of his regular trade. Even the practice of selling second grades or so-called job lots at properly reduced prices may be considered justifiable only when the goods are indelibly marked for recognition as to second quality by the consumer.

There is no need to recite the entire list of tricky practices which the high-minded commercial men of North and South America condemn as individuals. These, however, might be carefully rehearsed and written down and by a process of studious analysis reduced to several fundamental prohibitions in principles on which Pan-American agreement could be expected. I would, however, be in favor of an explicit and detailed exhibit of those practices as the first step in formulation of the creed, so that the underlying principles would be thoroughly apprehended by those people who need daily direction in the same way that the great moralist Moses gave it to them.

Practically all instances of suspicion directed against a customer or competitor as to his motives would completely disappear if we knew that he had pledged himself to a code that we ourselves support.

Further, let me say that business should explain to the world the irresistible economic laws on which it is founded; it should encourage and advertise the superb morality of its directing heads; it should formulate and profess a creed appropriate to the commercial idealism of the day, and it might, with great profit, define a code of business honor which good business everywhere would gladly embrace for its own protection.

#### BUSINESS INTEGRITY TO REPLACE CREDITS DESTROYED BY WAR.

At this particular juncture of world affairs, when we may count the loss by war of \$250,000,000,000 worth of accumulated credit, representing the earnings of millions of people during the last century, we must look forward to commercial operations based on future earning capacity. The credits and the negotiable values

which were available to us in July of 1914 have been diverted to other uses or have completely disappeared. This is primarily true of Europe, but its effects are even now being directly felt in the new world. From now on commercial credits and confidence will be based, to a large degree, on the future earning power of the people in all parts of the world. Those countries which have been wholly occupied in warfare will be called upon to redeem the inflated currency issued by their governments; they will be called upon to produce raw materials and finished commodities in such volume that a surplus over their own normal needs will accumulate and be translated into financial credits. In other words, only a part of a nation's fiscal strength will be found in values now existing. Since our dependence for the resumption and expansion of commerce will depend very largely on the future ability of peoples to earn an excess livelihood, and since we must accept promises to pay at a future date instead of demanding immediate delivery of gold, we are in the position of relying on the moral integrity of business interests everywhere to make good their promises. Could any time, therefore, be more propitious for the formulation of moral values in business and for a complete comprehension and acceptance of a code of honor binding us closer together and making of the peoples within the realm of the Pan-American Union an economic unit working for their common salvation?

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#### A NEW FORM OF CALOMEL.<sup>1</sup>

A new method of preparing calomel in a bulky and therapeutically highly active form has been devised by Duret, and particulars of the new form are given in the "*Annales de l'Institut Pasteur.*" In view of the importance attached to the use of calomel, in the shape of an ointment and also of hypodermic injections, his process and conclusions are of particular interest. The method is based on the following reactions: Sodium bicarbonate reacts with magnesium chloride to form sodium chloride and magnesium bicarbonate. Hydrochloric acid (liberated by the reduction of mercuric chloride) reacts with the magnesium bicarbonate thus formed to yield, again, magnesium chloride; simultaneously the mercuric chloride present

<sup>1</sup> Reprinted from *The Chemist and Druggist*, June 7, 1919.

is reduced to mercurous chloride. The details are as follows: A solution of

Sodium bicarbonate .....	6 grams.
Pure glucose .....	10 "
Distilled water .....	80 "

is added to a solution of crystalline magnesium chloride, 7.5 Gms. in 20 Gms. of distilled water. This mixture is then added to the following solution, contained in a flask of 500 Cc. capacity:

Mercuric chloride .....	11.5 grams.
Hydrochloric acid (33.65 per cent.) .....	10 drops.
Distilled water .....	100 grams.

Carbon dioxide is liberated, while mercurous chloride is precipitated in a very finely divided state. To complete the reaction, the flask is heated on a water-bath, with constant agitation until no more gas is evolved. It is then allowed to cool, filtered, and the precipitated mercurous chloride is washed with cold distilled water. This formula yields about 10 Gms. of calomel, in a form three times bulkier than the ordinary preparation. The amounts given must be strictly adhered to, as an excess of magnesium bicarbonate would yield magnesium carbonate mixed with the calomel; while an insufficient amount of magnesium bicarbonate would result in leaving unchanged a portion of the mercuric chloride. Tests which were conducted by the author showed that the calomel obtained by this method is ionized in water to a greater extent than the ordinary product (tested with dîphenylcarbазid and sodium monosulphide), and for this reason its therapeutic activity is also greater. Experiments showed that this finely divided calomel, in the presence of organic substances, was dissociated into metallic mercury in a state of extremely fine subdivision; consequently by this method is it possible to employ mercury *in statu nascendi*, thus assuring its rapid absorption. For its application as calomel ointment the author gives the following formula:

Precipitated calomel (obtained by above process) ..	10	grams.
Crystalline magnesium chloride .....	10	"
Sodium bicarbonate .....	7	"
Thymol .....	0.15	"
Camphor .....	0.35	"
Arachis oil .....	15	"
Glycerite of starch .....	15	"
Anhydrous lanolin .....	20	"
Distilled water .....	25	"



The magnesium chloride, sodium bicarbonate and water are mixed in a mortar, the precipitated calomel added, and then the glycerite of starch. Melt by gentle heat the anhydrous lanolin in 10 Gms. of arachis oil, add the thymol and camphor previously dissolved in 5 Gms. of arachis oil, and while liquid add the whole to the first mixture, and heat until a homogeneous ointment is obtained.

For the hypodermic injection of calomel the following formula is given:

Mercuric chloride .....	5.75	grams.
Hydrochloric acid (33.65 per cent.) .....	5	drops.
Glucose .....	5	grams.
Sodium bicarbonate .....	3	"
Crystalline magnesium chloride .....	3.75	"
Distilled water .....	20	"
Syrup to .....	100	Cc.

Dissolve in a flask of 200 Cc. capacity the mercuric chloride, by warming, in the distilled water to which the hydrochloric acid has been added, then add the glucose. Mix, in a porcelain capsule, the sodium bicarbonate with about 50 Gms. of syrup, add the magnesium chloride and mix. Now add the mixture to the contents of the flask. The capsule is repeatedly rinsed with small amounts of syrup, which are added to the flask. Shake and warm on a water-bath until the evolution of gas has almost ceased; allow to cool, and add sufficient syrup to produce 100 Cc. This yields 5 Gms. of calomel (1 Cc.=0.05 Gms. of calomel) in extremely fine subdivision, which keeps for a long time in suspension.

To avoid the pain which follows the injection of calomel, and which is due to the liberation of free hydrochloric acid, the following modification is employed:

Mercuric chloride .....	6.775	grams.
Hydrochloric acid (33.65 per cent.) .....	5	drops.
Glucose .....	5	grams.
Sodium bicarbonate .....	8.65	"
Crystalline magnesium chloride .....	10.5	"
Distilled water .....	25	"
Syrup to .....	100	Cc.

Of the above, 1 Cc. corresponds to 0.06 Gm. of calomel.

## QUANTITATIVE DETERMINATION OF OXYMETHYLANTHRAQUINONES.<sup>1</sup>

Four methods for the determination of the oxymethylantraquinones in such drugs as rhubarb, senna, etc., have been suggested. They are: (1) Spectroscopical, (2) colorimetric without colorimeter, (3) colorimetric with colorimeter, and (4) gravimetric by precipitation by azonitroaniline. The method now proposed depends upon the hydrolysis of the glucosides of the oxymethylantraquinones and the separation of the latter in such a state of purity that they can be weighed. As the glucosides are sensitive to heat, hydrolysis is effected at the boiling point of chloroform. The determination is effected as follows: A weighed quantity of the finely powdered drug (about 2 Gm. of rhubarb, 5 Gm. of senna), dried at 60°–70°, is introduced into a short-necked flat-bottomed flask and 200 Cc. of dry chloroform added; the whole is weighed and boiled under a reflux condenser for fifteen minutes. When quite cold the chloroformic solution is filtered off and the residual drug washed. The solution is shaken with a 5 per cent. solution of caustic soda, which is separated, washed with chloroform, acidified with hydrochloric acid, again shaken with chloroform, and the chloroformic solution separated, filtered, evaporated to dryness, and the residue weighed. This is the weight of the free oxymethylantraquinones. The residual drug (after boiling with chloroform) is carefully returned to the flask and made up to the original weight with chloroform. Fifty Cc. of 25 per cent. sulphuric acid are added, and the whole weighed. The mixture is then boiled on a water-bath for 2½ hours, shaking from time to time. After cooling, the weight is made up with chloroform, the whole transferred to a separating funnel, and about 150 Cc. of the chloroformic solution separated. This is shaken first with 50 Cc. of a 10 per cent. solution of sodium bisulphite, separated, and filtered through kieselguhr and shaken with 100 Cc. of 1 per cent. hydrochloric acid. One hundred Cc. of the chloroformic solution are then evaporated to dryness, and the residue weighed, from which the percentage of the combined oxymethylantraquinones can be calculated. Rhapontic rhubarb was found to contain 3.18 to 3.95 per cent. combined and 0.24 to 0.28 free oxymethylantraquinones, senna 1.98 to 2.12, total and cascara 1.32 to 1.47 total oxymethylantraquinones.

<sup>1</sup> *Journ. de Belgique*, 1, 200. Reprinted from *The Pharm. Jour. and Pharmacist*, April 26, 1919.

THE HESS HOME-MADE MILK REFRIGERATOR.<sup>1</sup>

Milk that is not kept cold is a dangerous food for babies. Every minute that the milk is much above the temperature of ice the germs of disease are increasing in it at an alarming rate. Very many babies die of summer complaint merely because they have been given milk that has stood for hours in a warm room. Keeping the bottle in a refrigerator containing a small piece of ice, does not make milk a safe food, for the temperature in these boxes is often 55 to 60 degrees Fahrenheit; that is, far above the freezing point.

Many mothers who have refrigerators are unable to buy enough ice in summer to preserve the milk in them for twenty-four hours. This should not be, for anyone can make at home a cheap but excellent milk refrigerator, requiring very little ice. A simple refrigerator of this kind uses less than five cents' worth of ice every day, keeps the milk below 40 degrees (that is near freezing point) so that mothers having one may be sure that the warm weather cannot spoil the baby's milk. Such an ice box is, therefore, economical, and protects the baby.

*How to Make One.*—Get a wooden box at a grocery store, such as a soap box, fifteen inches in depth. Buy a covered earthenware crock, tall enough to hold a quart bottle of milk. Also get a piece of oilcloth or linoleum about a foot wide and three feet long. Sew the ends together to make a cylinder which will fit loosely around the crock. Place the crock inside the oilcloth cylinder, and stand them in the center of the box. Now pack sawdust or excelsior beneath and all about them to keep the heat from getting in. Complete the refrigerator by nailing a Sunday paper or two other newspapers to the wooden cover of the box. *It is now ready for use.*

*How to Use It.*—In the morning as soon as you receive the milk, place it in the crock; crack five cents' worth of ice and place it about the milk bottle. Place the cover on the crock and the lid on the wooden box. No matter how hot the day has been, you will find some unmelted ice in the crock the next morning. Remove the crock every morning to pour off the melted ice.

<sup>1</sup> Reprinted from *Public Health News*, July (the monthly publication of the Department of Health of New Jersey).



## PHILADELPHIA COLLEGE OF PHARMACY.

### MINUTES OF THE QUARTERLY MEETING.

The quarterly meeting of the college was held June 30 at 4 P.M., in the library, president, Howard B. French, presiding.

President French reported the progress made toward securing an amendment to the charter of the college. Public notice had been given in the daily papers and the matter was entered in Common Pleas Court, Number 1192, June term, 1878.

Professor Charles H. La Wall for the delegates to the meeting of the Pennsylvania Pharmaceutical Association at Buena Vista reported. The meeting was particularly noticeable for the large number of the faculty of the college and members of the board of trustees in attendance, nine members of the faculty and seven members of the board were present. Philadelphia was also well represented. Thirty-seven papers were read, twelve of these being contributed by members of the college. The papers by Professor H. W. Youngken, Professor Joseph W. Ehman and Professor P. S. Pittenger were especially noteworthy. Real progressive work was accomplished, harmony prevailed, and the college has reason to be proud for its share in the proceedings. Professor Robert P. Fischelis, of the college, was elected president.

Mr. George M. Beringer for the delegates to the New Jersey Pharmaceutical Association, reported that the meeting was held at Atlantic City, June 10-13. Despite the many attractions that Atlantic City offers to lessen the attendance, the meetings were full of interest. Papers were read on popular subjects—Legislation, national and state, the Conditions of Pharmacy and other matters of interest were discussed. The New Jersey Association is the oldest of all the state associations and prides itself, justly, on this account. It will be fifty years old next year and the golden anniversary will be held in Newark, in which city the initial meeting was held. Mr. Edward A. Sayre, a former president, was again chosen president.

Dr. A. W. Miller, for the delegates to the Delaware Pharmaceutical Association, reported that the meeting was held at Wilmington on June 5. The association was a small one, and the attendance was lessened because of the scarcity of drug clerks. No scientific papers were presented, the meeting being mainly one for

business. After luncheon a visit was made to the Brandywine Cemetery, when Dr. Miller gave them a talk on the many remarkable trees and plants for which the cemetery is noted.

President French read from *Poulson's American Advertiser* of date December 29, 1821, a long advertisement inserted by the officers of the college, telling of existing evils in the drug trade of that time and outlining the first steps taken towards the formation of the College of Apothecaries (the early name for the college); also a lengthy advertisement along the same lines from the *National Gazette*, three years later. The reading was eagerly listened to by the members.

Professor H. W. Youngken presented two specimens of the *Colocasia esculenta*, commonly called "dasheen." The plants had been cultivated in the roof garden of the college. The tubers are used as food, like the potato, in the tropics and some of the southern states.

Professor E. F. Cook said this was a fitting time to speak words of commendation for the improved conditions in the AMERICAN JOURNAL OF PHARMACY. He had heard many expressions of appreciation because of the high character and scientific interest of its contents.

Seven applications for active and one for associate membership were read and referred to the Committee on Membership.

The Committee on Membership presented a supplemental report giving the increase in members for the past three years. Continued efforts would be made to add to the gratifying increase of the past few years.

President French made the following appointments:

*Committee on Nominations.*—Charles H. La Wall, Wm. L. Cliffe, Joseph W. England, Charles F. Liebert, with E. F. Cook, chairman.

*Delegates to the Meeting of the American Pharmaceutical Association at New York, beginning August 25.*—Charles H. La Wall, E. F. Cook, J. W. Sturmer, C. B. Lowe, F. X. Moerk, F. P. Stroup, John K. Thum, H. W. Youngken.

*Delegates to the Conference of Pharmaceutical Faculties.*—Charles H. La Wall, F. P. Stroup, J. W. Sturmer.

C. A. WEIDEMANN, M.D.,

Secretary.

## ANNUAL MEETING OF THE NATIONAL PHARMACEUTICAL SERVICE ASSOCIATION.

BY E. FULLERTON COOK, *Secretary.*

The annual meeting of the National Pharmaceutical Service Association was held at 145 North Tenth Street, Philadelphia, on the evening of June 30, 1919.

The secretary presented his annual report, briefly reviewing the activities of the association. Attention was called to the many hundreds of petitions sent to the Committee on Military Affairs of the House of Representatives from all parts of the United States in the interest of the Edmonds Bill, together with many personal telegrams and letters from prominent pharmacists, physicians, parents of men in the military service, and many public men. Considerable newspaper activity was also secured in various parts of the country.

Although the Edmonds Bill did not pass in the last session of Congress, it has been reintroduced and arrangements are being made for a conference during the annual meeting of the American Pharmaceutical Association, so that all who are interested in securing such legislation may have an opportunity to express their views, and determine what modifications may be necessary. At this meeting there will also be considered the Naval Bill introduced by Hon. George P. Darrow, for the establishment of permanent commissions in the Hospital Corps of the Navy, and it is hoped that Congressmen Edmonds and Darrow, and officials of the Navy can be present to advise with and give us the benefit of their experience.

The treasurer presented his annual report, and in setting forth the finances of the association since its establishment, stated that the printing expenses have totaled \$555.56, postage \$394.59, expense of presenting the cause of military pharmacist to other associations \$178.55, and the cost of a stenographer in the office, \$807.50, with office furniture and typewriter rental \$29.95, these totaled an expenditure of \$1,966.15. The number of those who have failed to renew their membership since the signing of the armistice has been disappointing, and as shown by the treasurer's report, the necessary expenses in conducting this work is comparatively large.

The officers have given liberally of their time and services and it is strongly urged that the rank and file of pharmacy support the new officers in the propaganda which must be conducted actively during the present term of Congress if we can hope for success.



It is hoped that before the New York meeting of the American Pharmaceutical Association a conference can be held with the office of the Surgeon-General of the Army, so that the army viewpoint of such legislation can be properly presented at the meeting.

The reports from the Ohio Branch of the National Pharmaceutical Service Association were most gratifying and showed an intense interest in the cause of military pharmacists. About 200 members of this branch have recently renewed their allegiance and the activities of this branch were commended.

The election of officers for the ensuing year resulted as follows:

*President*—Dr. Frank Cain, Cincinnati.

*Vice-President*—Caswell A. Mayo, Cincinnati.

*Secretary*—E. Fullerton Cook, Philadelphia.

*Treasurer*—Josiah C. Peacock, Philadelphia.

*Executive Committee*—George M. Beringer, Camden, N. J.; Robert P. Fischelis, Philadelphia, Pa.; Eugene G. Eberle, Philadelphia, Pa.; William D. Robinson, Philadelphia, Pa.; Theo. D. Wettersstroem, Cincinnati, Ohio; Jeannot Hostmann, New York City, N. Y.; Henry Kraemer, Ann Arbor, Mich.; Charles H. LaWall, Philadelphia, Pa.; Edwin L. Newcomb, Minneapolis, Minn.

A motion of appreciation to the medical friends who have been helping the association in the effort to secure proper ranking for pharmacists in the army was unanimously approved. It was suggested that if possible, a meeting of the National Pharmaceutical Service Association be held at the New York meeting of the American Pharmaceutical Association and after the president's reception on Wednesday evening was suggested as an appropriate time. A committee consisting of Messrs. Hunsberger and Eberle were appointed by the president to audit the treasurer's accounts.

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## FRANKLIN MUHLENBERG APPLE, PH.G., PHAR.D.

BY JOSIAH C. PEACOCK.

The many friends of the subject of this sketch were severely shocked by the news of his sudden demise at his late residence in Philadelphia, on the morning of July 9.

Franklin Muhlenberg Apple was a son of the late Reverend B. F. Apple and Ella P. Apple, and was descended from sturdy an-

cestry on both sides. He was born at Centerville, Northampton County, Pennsylvania, on February 14, 1870. He graduated from the Bangor High School, Bangor, Pa., in 1885, and immediately thereafter entered the drug business.

Later, he came to Philadelphia and engaged himself with his cousin, the late Milton S. Apple, in whose pharmacy he remained during his college course. He matriculated at the Philadelphia College of Pharmacy in 1888, and graduated from this institution in 1890. He was awarded the Alumni Association Prize Certificate for the highest percentage shown by his class in the recognition of specimens; and this award carried with it the additional honor of being the highest mark attained to that time in the competition for this prize.

As a student, he was eager to learn and anxious to apply. His thesis, "Glycerita," was selected by him as a means to apply and profit by the instruction which he had received. The writer first met him as a neighbor on the benches of the Philadelphia College of Pharmacy, and then appraised him as a youth of steadfast purpose and of sterling qualities; and an acquaintance of over thirty years has only served to strengthen that opinion.

In the autumn of 1890 he was engaged by Professor S. P. Sadtler as assistant in the Chemical Laboratory of the University of Pennsylvania, and here he continued until the following spring, when he purchased a drug store at Seventeenth and York Streets, this city.

In 1894 he married Mary E. Hess, of Centerville, Pa., and her practical ability has always been a great help to him. His conscientious efforts as a pharmacist were soon rewarded, for he rapidly built a substantial business, and soon acquired a second store.

But his strength was not equal to the burden which he had assumed and because of ill health he decided to dispose of his stores and try another occupation; accordingly he sold his business in 1899.

For somewhat over a year following this change, he was a representative of the Horlick Company in Philadelphia, and during this time he was studying the relations between physicians and pharmacists; all the while gathering much information during his visits to the medical practitioners. This experience led him to give much careful thought to the matter of refilling prescriptions. But his problems were too intimately connected with the actual practice of pharmacy to be perfected outside of it, and they brought him back

into the service in 1901, at which time he bought the pharmacy at Thirty-first and Berks Streets, Philadelphia. Here he put into practice many of the things with which he was deeply concerned. Among these was his "Square Deal Prescription Blank," so arranged that the physician would clearly show a willingness or objection to a renewal. And it is conceded that his efforts along this line proved to be a great impetus toward a better understanding and regulation of the refilling of prescriptions. He devoted much time and labor to the propaganda on U. S. P. and N. F. preparations which the newly appearing revisions of these authorities made quite desirable at that period.

He was a member of the Pennsylvania Pharmaceutical Association, the American Pharmaceutical Association, also its Philadelphia Branch, and of the National Pharmaceutical Service Association. During the time he was a proprietor he was a member of the Philadelphia Association of Retail Druggists and of the National Association of Retail Druggists.

From the date of his return to the art, he showed his real interest in it through his contributions to pharmaceutical literature. These were numerous and covered a wide range of subjects. He was awarded the Pennsylvania Pharmaceutical Association prize for one of his papers. He was active in the committee work of the various associations. He was Chairman of the Section on Practical Pharmacy and Dispensing of the American Pharmaceutical Association in 1907-1908; chairman of the Section on Commercial Interests, of the same body, in 1910-1911; first vice-president of the American Pharmaceutical Association in 1913-1914; and a member of the council of that organization for several years thereafter. His activities and appeals for the elevation of pharmacy attracted the attention of the Department of Pharmacy of the Medico-Chirurgical College, and he was invited to give instruction there upon the subject of compounding of prescriptions. The careful thought and painstaking efforts with which he conducted this course were recognized by the College, which in 1912 conferred upon him the honorary degree of doctor of pharmacy; while the alumni association of the same school made him an honorary member. But again overtaxed by the constant work and the anxious responsibilities of pharmaceutical service, he succumbed to ill health a second time, and, in 1914, disposed of his business; a move which he very much regretted to make, although he believed that he should from sheer



physical necessity relinquish the work in which he had been so deeply interested. This inability to pursue his chosen labor was known to have been a keen disappointment to him.

Realizing now that he must look for strength and health he put his attention upon athletic and out-of-door exercises; and among other associations devoted to physical welfare, he was at different times a member of the Belfield, Bon Air and Cobb's Creek Golf Clubs. His mind however was not satisfied with these affairs except as recuperative measures; his interest in pharmacy continued uppermost.

At this juncture the work of the Red Cross attracted his attention and enlisted his sympathy and zeal; and for a year and a half he served with Auxiliary No. 13. Here his nicety of work was greatly appreciated, and his conscientious efforts toward improving and standardizing methods and products endeared him to all with whom he came in contact.

As his health was severely tried by the winter climate of his home city, he decided to reside in Florida during the cold months; and from this sojourn his health derived benefit.

Having returned to Philadelphia in the spring of 1918, he determined to render some service closely associated with the needs of the fighting force, so he applied at the Eddystone Works, and for several months was an inspector on rifle work. But the opportunity which his patriotic spirit sought, wherein to do something to help win the war, came when he was appointed inspector of scales at the Woodbury Bag Loading Plant, Woodbury, New Jersey. In this capacity, his trustworthiness and readiness to accept responsibility were soon recognized and he was rapidly promoted to the position of chief of ballistic data and stencils. His services, rendered purely from patriotic motives, were of such satisfactory nature that he was given a testimonial letter in recognition of them, by the officer in charge, and also awarded a certificate "for his faithful services to the United States Government" by the chief of ordnance.

He served in the Fourth Liberty Loan Campaign at the same plant, and was instrumental in raising approximately \$65,000 among the government employees there.

The armistice having been declared and winter fast approaching, he sought again the balmy air of the South. Upon his former visit he had made many friends, and the esteem in which he was held by his fellow visitors is attested by his election as vice-president of the

Pennsylvania Society of St. Petersburg, Florida. There during the past winter he occupied his time in muscular exercises both of an athletic and of a practical nature, as he not only won prizes in the St. Petersburg Lawn Bowling and Sunshine Club contests, but also found so much real pleasure in the mechanical work of building a new home of his own, that spring had come again almost before he was aware. Convinced now that he had found relief in the climate of that locality, he decided to permanently locate in St. Petersburg, and with this plan in mind he and Mrs. Apple had returned to Philadelphia and were busily engaged with affairs pertaining to their removal in the early autumn, when the end came.

So stand his works more impressive than words. But I, his friend since early days, who knew so well that his ambition was limited by his strength of body, would like to say, in parting, these few words: Franklin Muhlenberg Apple was a sincere, genuine being; he could not, much less would he, dissemble; 'twas not his nature; he must be himself. And though his temperament throughout life seemed one of intense earnestness, it was because he ever had and showed the courage of his convictions to stand for things in that light of the right in which he saw them. He had a jolly side, as well; a cordial hand shake, a hearty laugh, a real, loyal interest in his friends, a tender heart, a generous disposition, and he was deeply appreciative.

One of the pleasing thoughts of his life was that he had made his own way from boyhood on.

He was a member of Meade Commandery, P. O. S. of A.; Linwood Assembly, No. 7, A. O. M. P.; and Eagle Council, No. 3, Fraternal Patriotic Americans. The funeral services were held on Friday evening, July 11. The interment was at Centerville, Pa., on the following day.

He is survived by Mrs. Apple, and his mother and three brothers.

## CURRENT LITERATURE.

### SCIENTIFIC AND TECHNICAL ABSTRACTS.

TEICHMANN'S HÆMATIN CRYSTALS.—Several methods have been proposed for simplifying this somewhat uncertain test. Bokarius finds that the best reagent is a mixture of glacial acetic acid (3 vols.) and saturated aqueous solution of sodium chloride (1 vol.). The suspected spot is moistened with three or four drops of the reagent, the liquid pressed out on to a slide, covered with a cover-slip, and heated to boiling; or a little of the substance may be scraped off on to a slide, the reagent added, and then covered and heated. No special precautions are necessary. (*Pharm. Weekbl.*, 55, 1502, through *The Pharm. Jour. and Pharm.*, April, 1919.)

DELICATE REACTION OF APOMORPHINE.—Gugliamelli's reagent affords an extremely delicate method of detecting apomorphine. The reagent is prepared by boiling 10 Gms. of sodium tungstate, 2 Gms. of sodium molybdate and 10 Gms. of pure arsenic acid with 70 Cc. of water for 1–2 hours under a reflux condenser, cooling, and adding water to 100 Cc. One or two drops of the alkaloidal solution and 1–2 Cc. of the reagent are shaken together for 3–5 minutes, and 5–10 Cc. of cold saturated solution of sodium carbonate added. The mixture develops an indigo-blue color. After again shaking, it is divided into two portions: one is shaken with amyl alcohol, which assumes a blue color, and the other with benzene, which is colored violet. (*Pharm. Centralb.* through *Schweiz. Apoth. Ztg.*, 57, 34, through *Pharm. Jour. and Pharm.*, April, 1919.)

IMPROVED METHOD FOR ESTIMATION OF SUGAR IN URINE AND BLOOD.—Cambridge advises that when a urine is expected to contain a low percentage of sugar, under 0.5 per cent., and with all blood and other fluids containing smaller amounts, the water to which the iodine solution is to be added should be boiled thoroughly to expel dissolved air and cooled immediately before the estimation is to be made. It is also advisable that the alkaline copper solution for sugar estimations with urine should be boiled in a small conical flask provided with a loose funnel as a stopper instead of in a beaker, and that the required amount of urine would be run into the boiling fluid from a pipette when the air dissolved in the solu-



tion and contained in the flask has been expelled. With blood, etc., the 7.5 Cc. of filtrate and 1 Cc. of sodium carbonate solution are boiled together in a similar way in a small conical flask fitted with a funnel-stopper, and the 1 Cc. of modified Benedict solution is added after they have boiled for a few seconds. The water used for diluting the iodine solution and for washing out the flask, etc., should have been recently boiled and cooled. With these additional precautions the method gives uniformly reliable figures, even with the small amount of sugar in normal urine and blood. (From *Lancet*, London, May, through *Journal American Medical Assoc.*, June 28, 1919.)

DILUTE FLUORESCEIN SOLUTIONS FOR THE DETERMINATION OF OZONE.—When air containing very minute traces of ozone is shaken with a 1:1,000,000,000 solution of fluorescein, the fluorescein is destroyed, and the color is discharged. If stronger solutions of the dye are used, only the fluorescence disappears: a yellow solution remains. Oxygen and other oxidizing agents do not act thus. The reaction is not only more sensitive for ozone than any of the hitherto published tests, but it is quantitative. Two molecules of ozone will discharge the fluorescence of one molecule of fluorescein. The trace of ozone detectable in this manner is, therefore, practically one third of the quantity of fluorescein acted on. Thus, 3 mils of the 1:1,000,000,000 solution is equivalent to practically 0.001 Mgm. of ozone. Since the fluorescence of 1 mil of the solution is distinctly visible, the degree of sensibility of the reaction is evident; it greatly exceeds that of the familiar starch and potassium iodide test paper. (L. Benoest, *Comptes rend.*, 1919, 168, 612; from *The Pharm. Jour. and Pharmacist*, June 28, 1919.)

## MEDICAL AND PHARMACEUTICAL NOTES.

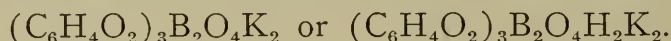
ISOTONIC EYE LOTIONS.—A solution of sodium chloride containing 14 Gms. in a litre is isotonic with the lachrymal secretion, and it has been proved that a solution of this strength is best borne by the corneo-conjunctival epithelium. A reduction must be made for the amount of any medicament that may be added, and this is ascertained in the usual way, viz., by dividing the molecular weight of sodium chloride by that of the medicament and multiplying by the

weight of the latter used. It must be remembered that one molecule of atropine sulphate is equivalent to two of sodium chloride. In the case of zinc sulphate and copper sulphate, sodium sulphate should be substituted for sodium chloride in the proportion of one of each of the sulphates for two of the chloride, and in the case of silver nitrate sodium nitrate should be substituted for the chloride. (*Jour. de Pharm. de Belgique*, 1, p. 201, through *The Pharm. Jour. and Pharmacist*, April 12, 1919.)

ISOTONIC HYPODERMIC INJECTIONS.—Although it has been shown that solutions of sodium chloride varying in strength from 0.6 to 2 per cent. can be injected hypodermically without apparent harm, it is desirable to make hypodermic solutions as nearly as possible isotonic with human blood serum. Hattie has calculated the percentage of sodium chloride that must be added to certain alkaloidal solutions in order to obtain this result, and has also determined by experience the quantity actually necessary; these figures show, as might be anticipated, certain differences. The following are the percentages of sodium chloride that must be added to the alkaloidal solution, as determined by actual experiment: *Morphine hydrochloride*, 1 per cent., 0.76; 2 per cent., 0.62; 3 per cent., 0.43; 1 per cent. + scopolamine hydrobromide, 0.02 per cent., 0.73. *Cocaine hydrochloride*, 1 per cent., 0.74; 6 per cent., 0; 0.75 per cent. + *adrenalin*, 0.005 per cent., 0.79. *Pilocarpine hydrochloride*, 3 per cent., 0.22. *Novocaine*, 1 per cent., 0.69; 2 per cent., 0.51; 1 per cent. + *adrenalin*, 0.005 per cent., 0.65; 2 per cent. + *adrenalin* 0.005 per cent., 0.47. *Eucaine*, 1 per cent. + *adrenalin* 0.005 per cent., 0.67. *Atropine sulphate*, 1 per cent., 0.79. *Emetine hydrochloride*, 1 per cent., 0.82; 3 per cent., 0.66; 5 per cent., 0.45. *Arecoline hydrobromide*, 0.5 per cent., 0.80. (*Pharm. Weekbl.*, 55, 202, through *Pharm. Journ. and Pharm.*, April 12, 1919.)

THE FATE OF QUININE IN THE ORGANISM.—At most, 40 per cent. of the administered quinine is excreted in the urine and feces; the rest is not deposited in the organs and must, therefore, have been destroyed. After intravenous injection the amount in the blood sinks rapidly, then more slowly to zero but oral administration gives a more constant quinine level which is retained for about twenty-four hours. (H. Hartmann and L. Zila, *Arch. exp. Path. Pharm.*, 83, 221-234, 1918.)

THE SALTS OF THE COMPLEX ACID: CATECHOL-BORIC ACID.—Two metallic and ammonium salts were prepared by shaking concentrated solutions of boric acid, catechol, and the respective hydroxide together in the molecular proportions 1:2:1. The three salts separated in the form of white leaflets. Similarly salts of organic bases were prepared and crystallized in needles. Ammonium salts;  $(C_6H_4O_2)_3B_2O_4(NH_4)_2$ ; potassium salt;



The aniline, dimethylaniline, and p-chloraniline salts are described. (J. Böeseken (with A. Obreen and A. van Haeften), *Rec. trav. chim.*, 37, 184-194, 1918.)

J. F. C.

*Note.*—Considering their constitution, the above described salts ought to be of value in the treatment of certain skin diseases and deserve pharmacologic investigation. The number and efficacy of available remedies for cutaneous affections certainly could not prejudice us against new and promising drugs.

J. F. C.

QUISQUALIS INDICA, A SUBSTITUTE FOR SANTONIN.—Davenport finds that an ancient Chinese drug called Shih-chün-tzŭ, prepared from the seeds of *Quisqualis indica*, a satisfactory substitute for the more expensive santonin. (C. J. Davenport, *China Med. J.*, 32, 133 (1918); *C. A.*, 12, 2404, 1918.)

J. F. C.

GENTIANA ASCLEPIADEA AS A SUBSTITUTE FOR GENTIANA LUTEA.—*Gentiana asclepiadea* L. contains only half as much total bitter substances as *G. lutea*; it contains less gentiopicrin than earlier reported. If it is to be used as a substitute for *G. lutea* twice as much must be taken to produce the same effects. Gentiopicrin is not a cure for malaria. (O. Hoyer and R. Wasicky, *Pharm. Post*, 51, 145.)

J. F. C.

CASTOR OIL IN DERMATOLOGY.—The value of castor oil in dermatological practice is the subject of a communication by D. W. Montgomery (*Jour. Cutan. Dis.*, 1918, 36, 466; Sept.). He points



out that the oil is very heavy and resistant to changes in temperature; thus it withstands heating better than most oils, and only solidifies when a very low temperature is reached. Some features of importance to dermatologists are: (1) Its solubility in alcohol. Various medicated alcoholic lotions are frequently employed in the treatment of the scalp, and without the addition of a small quantity of oil the spirit would in a dry scalp dissolve out an excessive quantity of sebum. For this purpose castor oil is the oil which is usually chosen. (2) This oil also facilitates the solution of salicylic acid in oils and ointments, and thus renders it less irritating to the skin. The salicylic acid must first be mixed with a little hot castor oil, and then added to the other ingredients. (3) Lastly, the internal administration of the oil acts particularly on the ascending colon, and as many of the more active skin reactions are caused by poisons generated in the *caput coli*, a favorite localization for the anaërobic proteolytic bacteria, it thus produces a clean alimentary canal, which in turn conduces to a clean cutaneous surface. (*The Prescriber*, April, 1919.)

ARSENOBENZOL: VALUE OF ADRENALIN (*Paris méd.*, 1918, 8, 81; Feb. 2).—G. Milian thinks that adrenalin, if properly administered, has the power to prevent the disagreeable by-effects of arsenobenzol. He recommends the administration of 2 mg. (2 Cc. of a 1:1,000 solution) by mouth, one hour before an injection, repeating the dose five minutes before and one hour after the injection. When a patient is intolerant of arsenobenzol, he advises the administration of one Mg. by mouth, morning and evening, for four days. To prevent crisis, congestion of face, vomiting, etc., a subcutaneous injection of one Mg. and an intramuscular injection of 0.5 Mg. should be given five minutes prior to the arsenobenzol. (See also *Prescriber*, 1918, p. 78.) O. Nageli (*Corresp.-Bl. f. Schw. Aerzte*, 1917, 97, 1291, *per Endocrinology*, 1918, 2, 467; Oct.-Dec.) has reported a case in which adrenalin proved useful in combating a marked exanthema, which appeared after administration of a small dose of novarsenobenzol. A hypodermic dose of adrenalin (0.5 Cc. of solution for 0.3 Gm. of novarsenobenzol) given a few minutes before the arsenical injection, entirely prevented the cutaneous reaction.

B. B. Beeson (*Amer. Jour. Syph.*, 1919, 3, 129; Jan.) believes

that suprarenal insufficiency is the determining factor in the production of certain reactions following administration of arsenobenzol, and gives one Mg. intramuscularly ten minutes before the intravenous injection. In cases presenting marked nitroid crisis he does not hesitate to give double that amount.—T. S. (*The Prescriber*, May, 1919.)

ARSENOBENZOL: DECOMPOSITION OF SOLUTIONS (*Jour. Lab. and Clin. Med.*, 1919, 4, 181; Jan.).—J. B. Rieger says that arsphenamin (American arsenobenzol or salvarsan) may contain an arseniuretted methyl compound, which decomposes with liberation of cacodyl-like substance. Some preparations give a garlic-like odour when dissolved, others develop it after standing in solution for some time. According to the amount of this that may have accumulated, along with other factors, a reaction may occur after injection, marked by fall in blood pressure, dyspnoea, and cyanosis. The author suggests that the use of methyl alcohol in its preparation should be avoided.—T. S. (*The Prescriber*, May, 1919.)

COPPER SULPHATE IN DERMATOLOGY.—Several formulæ for the use of the copper sulphate in various skin diseases are given by De Herain (*Presse méd.*, Oct. 31, 1918). For parasitic affections he recommends a strong ointment:

Copper sulphate .....	2
Zinc oxide .....	15
Lanolin .....	10
Soft paraffin .....	73

For milder complaints, such as acne, eczema, etc., a weak ointment containing only 0.2 per cent. of copper sulphate is prescribed. A dusting powder containing 0.2 (weak) or 2.0 (strong) per cent. of copper sulphate in talc may be used. In eczema he uses a lotion containing 0.01 per cent. of the salt dissolved in water, and after cure, to avoid relapses, continues with a solution 0.0025 per cent. (*The Prescriber*, May, 1919.)

CONSTIPATION.—J. Ritchie gives the following formula in an article on the subject (*Edin. Med. Jour.*, 1918, 21, 253; Nov.):

℞ Ext. cascar. sagrad. liq.....	5i
Paraff. liquid .....	5iiss
Ext. malti liq. ....	5iiss

M. Sig.—“A teaspoonful twice daily.”

(*The Prescriber*, May, 1919.)

AN INCOMPATIBILITY.—The following prescription is incompatible:

R̄ Magnes. calc. ....	gr. x
Salol. ....	gr. v
Acid. acetyl-salicyl. ....	gr. v

In the presence of moisture the magnesia will combine with the acetyl-salicylic acid and the salol will decompose into magnesium salicylate and phenol.—J. A. M. A. (*The Prescriber*, May, 1919.)

ACRIFLAVINE AS A WOUND DRESSING.—Many surgeons have expressed disappointment in the results gained from the use of a solution of 1:1,000 of acriflavine in normal saline as a dressing for wounds. Thomas E. A. Stowell (*B. M. J.*, 1919, 1, 244; Mar. 1) confirms these unsatisfactory results, but has found an emulsion, if properly prepared, most effective. His formula is as follows:

Acriflavine .....	0.1
Thymol .....	0.005
White wax .....	4.0
Liquid paraffin .....	76.0
Distilled water .....	20.0

Much skill and care are necessary in the preparation of this emulsion and the presentation of it in a sterile condition. He has used it for broken-down tuberculous glands, and for smearing over abdominal wounds after closure of the peritoneum where there has been suspicion of soiling; in this way drainage tubes and their resultant bad effects can be avoided.

The following paste is recommended by A. H. Tubby *et al.* as an application for gunshot wounds (*Lancet*, 1919, 1, 251; Feb. 15):

Bismuth carbonate .....	25
Paraffin (soft) .....	75
Acriflavine .....	0.5

Bismuth carbonate is, they find, less toxic than the subnitrate. (*The Prescriber*, May, 1919.)

BURNS: MAGNESIUM SULPHATE SOLUTION (*Jour. Pharmacol. band Exper. Therap.*, 1918, 12, 211; Nov.).—S. J. Meltzer, in course of a research on the action of magnesium sulphate on the



nervous system, found that a concentrated solution had a very favorable effect when applied to scalds and burns. Burns of the second degree are invariably arrested in their development when such a solution is applied early, while those of the third degree run a more favorable course under this treatment than under any other method. A solution of 25 per cent. strength, or even stronger, should be used. (From *The Prescriber*, May, 1919.)

WOUNDS: PARAFFIN TREATMENT (*British Med. Jour.*, 1919, 1, 243, Mar. 1).—E. F. Pratt confirms the advantages of paraffin in the treatment of burns, as testified to by Hull and by Haig. Several cases are described, which the author states were under observation from start to finish. The majority were cases of lacerated wounds: in some "ambrine" was used, in others No. 7 paraffin. The technique is carefully detailed, the essentials of which are cleansing with sterile water and spraying on the melted paraffin. One layer of gauze is put over this, then a cotton-wool pad and a bandage. This is retained for twenty-four hours; five dressings are usually sufficient to effect a cure. The author states that the objections to "bipp"—expense, toxicity, and interference with x-ray work—do not apply to paraffin. He is of the opinion that the active ingredient in "bipp" is the paraffin, iodoform never having given satisfaction in the past, while bismuth is inert.—P. A. H. (*The Prescriber*, May, 1919.)

IMPORTANCE OF FATS IN THE ASSIMILATION OF ALBUMINOIDS.—The author has previously shown that in the presence of fats the toxicity of albuminoids of food is diminished and their nutritive value is increased. When fat is present the minimum quantity of albumin necessary to maintain weight is only about one third that required when starch replaces fat. The amount of starch-albumin ration necessary to maintain weight contains about one fourth more calories than a similar fat-albumin ration. It has long been known that the administration of fats, and especially oil-containing seeds and milk, assists assimilation. This was formerly attributed to the stimulation of the digestive secretions by the fat. But this explanation is not sufficient. Fats intervene in the synthetic reconstruction of protein molecules. Maillard has shown that glycerin acts as a condensing agent with the amino-acids. The author finds

that it acts on the  $\text{—CO—NH—}$  linkage which occurs in the amino-acids of protein molecules. It also plays an important part through its alcohol function, being temporarily esterified and then saponified. The sugars, as polyatomic alcohols, probably play the same rôle. Probably, however, the importance of these properties of glycerin are secondary to those of the fatty acids. It is known that fatty acids may be formed from proteins, such as casein. Probably the reverse action occurs in the organism. Baudi has demonstrated that fatty and amino-acids combine, forming lipoproteids, in which the physical and chemical properties of the fats are completely masked. Thus it is probable that the fatty acids combine with the residues of the amino-acids derived from ingested albumins, and thus render them assimilable. This explains the favorable action of the fats on the digestion of albuminoids, and also the observed benefit which follows the administration of such fats as cod-liver oil in cases of malassimilation of nitrogenous foods, in diabetic or tubercular cachexia. (F. Maignon *Comptes rend.*, 1919, 168, 626, from *The Pharm. Journal and Pharmacist*, June 28, 1919.)

## TRADE INTEREST.

EGYPTIAN OPIUM.—The area devoted to the cultivation of the opium poppy in Egypt has varied from 5,000 acres in 1833 to 1,500 acres in 1917. The plant cultivated is usually the variety with white petals, but the one with red flowers is also grown. The chief localities are the islands of Upper Egypt, which are covered by inundations. The seed is sown between the middle of October and the end of November, the harvest taking place in the following February and March. The inspissated juice is collected by knives moistened with saliva, transferred to shells, plates or poppy leaves, and, after about a fortnight's drying, made into cakes weighing from 15 to 250 Gm., which are then further dried. Cakes of 300 to 500 Gm., and sticks 20 to 30 Cc. long, wrapped in red paper, in imitation of Persian opium, are also found in the markets, but these are adulterated. The usual morphine content is 7 per cent., but 10 per cent. is not uncommon, and even 12 to 15 per cent. has been found. The cultivation is free, but trading in opium was prohibited except by certain authorized merchants. These authorizations were withdrawn in 1913. None is exported. It is, however, sold clandestinely.

tinely. (*Repert. de Pharm.*, 74, p. 345, through *Pharm. Jour. and Pharm.*, April 12, 1919.)

SEYCHELLES CINNAMON OIL.—In the course of a short article on the planting prospects in the Seychelles, a correspondent in the "Times Trade Supplement" states that a representative of one of the leading chemical firms in this country has recently returned from a visit to Mahé, the principal island of the Seychelles group, where he went to report on the possibilities of the local cinnamon-leaf oil industry. He has reported so favorably that, as a result, an important contract has been arranged between his firm and the Seychelles Rubber and Coconut Plantations Co., Ltd., for a regular supply of the oil extending over a number of years. Special kinds of still apparatus have been ordered and are being made in England for distilling purposes, and directly they are ready for use the oil will be produced on a large scale. As cinnamon-leaf oil enters into the composition of innumerable medicines and chemical mixtures, the future of this industry in the Seychelles is now assured. (From *The Chemist and Druggist*, June 28, 1919.)

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## CORRESPONDENCE.

### WHO WILL BE THE LEADER?

TO THE EDITOR:

Your editorial appeal of June "Who will be the Leader?" is interesting. In the opinion of this writer there is a way to accomplish the end desired and at the same time help to place the art of pharmacy on a substantial professional base.

There can be no doubt in the mind of the thinking, observing druggist that the one safe way to reach the goal of consideration "a professional man" is to so arrange his activities that they be really helpful to the practitioner of medicine. There is no good reason why a druggist should not regard himself the helper or subordinate of the doctor, and there is no good reason why the doctor should not accept him as such in good faith and establish relations that would redound to the credit and advantage of both. The profession of medicine includes that of pharmacy and it is only a matter of convenience to the doctor to tolerate the pharmacist in the capacity of independent helper.



There is a section of pharmacy and materia medica in the American Medical Association. Why not make that section one of activity and importance? This writer can not see anything at all inconsistent in a union with or absorption of the American Pharmaceutical Association by the American Medical Association. Why not make the American Pharmaceutical Association the section of Materia Medica and Pharmacy of the American Medical Association?

This writer does not anticipate the many objections possible of advancement by druggists who will not agree with him and passes directly to an exhibition of advantage to the druggist. (1) Standing as a professional man; (2) elimination of undesirables; (3) attainment of rights, no matter where or how employed.

As members of a section of the American Medical Association, registered pharmacists will have the full weight of authority and the influence of that association back of everything demanded.

The final outcome would be (a) separation of mere commerce from the art of the pharmacist; (b) licensing of pharmacists by a national board under the control of the American Medical Association; (c) advancement of the practitioners of the art to a position in society commensurate with service rendered.

—*Old Time Pharmacist.*

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## NEWS ITEMS AND PERSONAL NOTES.

THE DEGREE OF DOCTOR OF PHARMACY CONFERRED ON DEAN LA WALL.—At the annual commencement of the University of Pittsburgh on June 13, the honorary degree of doctor of pharmacy was conferred upon Professor Charles H. La Wall, dean of the Philadelphia College of Pharmacy, and successor to the late Professor Jos. P. Remington as chairman of the Committee of Revision of the U. S. Pharmacopœia.

PENNSYLVANIA BOARD OF PHARMACY.—The Pennsylvania Board of Pharmacy announces that as a result of the examinations held on June 6 and 7, 121 out of the 170 applicants successfully passed the tests for registration as pharmacists, and that out of the 132 who took the examination for certificates as assistant pharmacists 68 passed the examination. The next examinations will be held in the

Williamsport High School on Friday and Saturday, August 29 and 30. Applications should be sent to L. L. Walton, Secretary, P. O. Box 265, Williamsport, Pa.

NATIONAL EXPOSITION OF CHEMICAL INDUSTRIES.—The Fifth National Exposition of Chemical Industries will be held this year in Chicago during the week of September 22. The exhibition will be in the Armory of the First Regiment. The committee having charge of this exposition is a very representative one composed of officials and chemists of many of the leading chemical industries and editors of the leading chemical journals, and is under the chairmanship of Dr. Charles H. Herty. The personnel of the committee assures in advance that this, the fifth exposition of this kind, will be another great success.

DR. HENRY KRAEMER, DEAN OF THE SCHOOL OF PHARMACY, UNIVERSITY OF MICHIGAN.—After thirty-three years of service as a teacher in the Pharmacy Department of the University of Michigan, Professor Alviso B. Stevens has retired from active service and removed to a country life in California. Since the illness and decease of Professor Schlotterbeck, Professor Stevens has filled the position of dean of this institutional department. The vacancy in the deanship caused by his resignation has been filled by the selection of Professor Kraemer as dean.

A MEMORIAL TABLET IN HONOR OF PROFESSOR WHITEHEAD.—At the annual commencement exercises held on June 2, the alumni of the school of pharmacy presented to the South Dakota College of Agriculture and Mechanic Arts, a bronze memorial tablet to honor the memory of the late Professor B. T. Whitehead whose decease occurred on April 1, 1917.

For a period of twenty-one years Professor Whitehead was head of the department of pharmacy of this state college and is said to have been a very thorough, painstaking instructor.

THE N. A. R. D. CONVENTION.—The National Association of Retail Druggists will hold its convention at Rochester, N. Y., September 7-13. The pre-convention arrangements as announced give every evidence that the "Flower City" is doing its best to provide

for the comfort and entertainment of the members and delegates who attend this gathering of retail druggists. The numerous industries, of more than local fame, located in Rochester that will invite the visitors to inspect their plants, the beauty of the many city parks, the display and exhibition, all the booths of which have been taken by exhibitors, the entertainments provided, are promises of enjoyment. In addition many questions of vital importance to the drug interests must be considered at this convention. Among these may be mentioned, the dispensing of liquors as medicines, the traffic in narcotics and its elimination, price maintenance, etc.

PHILADELPHIA-MADE GOODS EXHIBITION.—An exhibition of the industries of Philadelphia will be held in the First Regiment Armory, Broad and Callowhill Streets, during the week of September 8-13. No other city can boast of such a wide range of manufactures, and these have earned for the City of Brotherly Love the title of the "Workshop of the World." It will be no small task to gather under one roof in such an exhibition the thousands of products manufactured in the industrial plants of the city. The purpose of the exposition is to demonstrate the commanding position of Philadelphia as the "Market Place of America."

THE NATIONAL TUBERCULOSIS ASSOCIATION.—In a circular issued by this national organization it is stated that tuberculosis annually causes 150,000 deaths in the United States. To the best of present-day scientific knowledge, the disease is not inherited. Infection, it is now believed, generally takes place during childhood.

Examination of men for the National Army revealed that tuberculosis is far more prevalent in this country than even the best informed authorities were aware. The official records show that almost 100,000 men were rejected because they were suffering from unsuspected implantation of the germ.

Tuberculosis has increased enormously in Europe. As the food supply fell off tuberculosis increased.

The seriousness of the situation calls for redoubled efforts and a nation-wide educational campaign. Plans are being formulated for the carrying on of such an energetic campaign during the months of October, November and December. This association depends to a large extent for its support upon the sale of the Red Cross



Christmas Seal, consequently unusual efforts must be put into the sale this year.

Many druggists have been aiding this worthy enterprise by assisting in the sale of these stamps and every druggist in the country should be willing to contribute, if nothing more, the time and energy required to make his store a successful sub-station for the sale of these seals.

BURROUGHS WELLCOME & Co.'s SUCCESSFUL FIGHT AGAINST A JAPANESE FRAUD.—After six years of expensive litigation in the Japanese courts, Messrs. Burroughs Wellcome & Co., the well-known London manufacturers of medicinal products, have succeeded in suppressing a fraud that was most deliberately planned and audaciously executed. A Japanese imitation of "Hazeline Snow," one of their toilet products, was offered for sale in China.

In preparation for the fraud the Japanese vendors endeavored to legalize their preparation by registration in Japan of three trade-marks associated with the genuine product. These registrations covered an imitation of the general design of the Burroughs Wellcome Label, specific details including the title "Hazeline Snow," and a copy of the Burroughs Wellcome & Co. Chinese label including their well-known "Unicorn" device trade-mark.

With the aid of the local British consuls, the sale of the spurious article was forbidden in various parts of China by means of local proclamations. Burroughs Wellcome & Co. have carried their suit to a successful issue and the Japanese Patent Court has invalidated the three trade-marks and further awarded to them the costs of the trials.

# THE AMERICAN JOURNAL OF PHARMACY

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SEPTEMBER, 1919

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## EDITORIAL.

### THE PRESIDENTIAL ADDRESSES.

The pharmacists of Great Britain and the United States are to be congratulated upon the addresses delivered by the presidents of their respective national pharmaceutical associations at the 1919 conventions. The sessions of the British Pharmaceutical Conference were held in London, July 22-23. The address of the president, William Kirby, M.Sc., is devoted almost entirely to a presentation of the need for research in pharmacy. The subject is treated in a masterly manner and the address evidences the careful thought and preparation of a scientific, educated pharmacist who has this subject at heart as well as in mind. As a literary production it, likewise, is a polished gem, even among such presidential addresses. As a gem it will bear study and use and the light from its trite truths, so clearly presented, must scintillate and create aspirations that will stimulate scientific investigations among the pharmacists of the English-speaking nations.

The need for the establishment of systematic research in pharmacy is common to both England and the United States and the statements of Mr. Kirby are as applicable to America as to Great Britain and a careful perusal of this address is urged upon all true pharmacists. The necessity for encouraging and fostering pharmaceutical research is plainly set forth as a duty of the government, of the captains of industry, as well as of the colleges of pharmacy.

He quotes the statement that had previously been made in the House of Commons regarding the German organization for research: "In the great chemical works in Germany, for every fifteen men employed in any category whatever there is one highly trained specialist and chemist, and that this industry is so important that

there is one highly trained specialist in chemistry for every forty-five employees in any category right throughout the whole range of industry."

In answer to the query he propounds, What are the reasons we do not trust in science sufficiently to put our money into making the necessary experiments? he advances as rejoinders: "The first is: the average business man knows so little about science that he is totally unable to value its certitudes. Therefore he must have a better and more serious education in it. The second is: our national weakness in believing that when the crisis comes in business or anything else our forceful character will ensure our winning through. Fortunately, English phlegm and courage, and the gift of doing best when things are at the worst, have availed once more to avert a catastrophe. Nevertheless, it is to be hoped that we shall not again handicap ourselves by indulging in such a magnanimous conceit. There is, I venture to think, also a third very important reason for our want of confidence in science as a daily tool. Our science students have not been consistently taught that the flower of the tree of knowledge, of all true science, is research. In other words, for the non-experimentalist, science without research is a jargon, and for the experimentalist a treadmill. The very kernel of all experimental and practical science is to learn how to solve the problems of nature and of art. No science student should be allowed to bear away any diploma or any degree from institution or university who has not spent a useful period in research work in some branch of science."

From the above we are justified in drawing certain conclusions. The American business man is evidently the possessor of the same general characteristics as are depicted for the English man of trade. The English tenacity, courage and "magnanimous conceit" are paralleled by Yankee ingenuity, daring and brag and both are in line for the same educational corrections, to avoid the same pitfalls. We are indeed glad to note the awakening in this respect that is apparent on both sides of the Atlantic Ocean. Many of the colleges in the United States have recognized the necessity for the training of their students in the methods of scientific investigation and research and it is anticipated that the time is not far distant when every university course will require that the graduation thesis of each student shall be an accurate description of some original research engaged in by the student.



Colleges of pharmacy have a duty in thus educating their students, which is imperative, and Mr. Kirby again accentuates the necessity for educating pharmacists on precisely the same lines, as far as physical and biological studies are concerned, as other men who are to be associated with them in research work.

Mr. Kirby is quite optimistic regarding the securing of financial aid for the aid of teachers and others engaged in pharmaceutical research. He says: "Surely means can be devised for the adequate remuneration of teachers and workers undertaking such work. Educated opinion throughout the civilized world is pulsing with a desire to realize the fruits of the tree of science now that it has been discovered by all and sundry. Pharmacy should take its part in this effort to enjoy the hitherto overlooked treasure. Its opportunity is to hand." Pharmaceutical leaders in America add their hearty endorsement to this adjuration and likewise to the project proposing coöperative research in institutions in which botanical, chemical, pharmacological and bacteriological work can be carried out.

The address of President LaWall of the American Pharmaceutical Association is likewise a presentation of subjects worthy of the careful consideration of pharmacists. While it deals, in the main, with problems that are peculiar to the association itself, many of its statements are of general interest to the progress of pharmacy and moreover the correction of defects in the management of the Association or the establishing of new methods and the advanced principles advocated will rebound to the benefit of pharmacy.

The formulating of a national code of ethics to be adhered to by members of the American Pharmaceutical Association will go along way toward the establishing of the profession of pharmacy and answering the uncalled-for criticism that at times are advanced against American pharmacy in toto.

The attitude of pharmacy in the reforms inaugurated by the anti-narcotic legislation and the recent coöperation with the Public Health Service regarding venereal diseases are considered as bearing tribute to pharmacy and as evidences of the true professional spirit by which private gain is subordinated to public welfare.

We are likewise in hearty accord with the presidential statement "that if added responsibilities should come to pharmacists through the issuance of rules and regulations in respect to both alcoholic liquors and narcotics, these should be accepted as a tribute to the dignity and responsibility of the calling and as a recognition of the

honesty and worthiness of the profession as a whole which is implied by such a trust."

Many of the other recommendations of this address of President La Wall are placed before our readers in the account of the meeting of the A. Ph. A. and it is hoped that the thoughts presented in these two admirable presidential addresses will receive the consideration merited and be made effective by appropriate actions.

G. M. B.

#### FURTHER RULINGS OF THE INTERNAL REVENUE BUREAU CONCERNING NON-BEVERAGE ALCOHOL.

The attention of druggists and manufacturers who are holders of permits to use or sell non-beverage alcohol is directed to the following additional rulings of the Internal Revenue. The efforts of all such holders should be directed toward the elimination entirely of alcoholic beverages or the surreptitious use for beverage purposes of preparations made for legitimate use as medicines, flavoring extracts, or toilet articles. Those who violate the provisions of these acts and regulations or who, as manufacturers or dealers, do not use every effort to prevent such frauds will assume a responsibility which may bring severe penalties as well as reflecting upon the position of the drug trade, every branch of which is endeavoring to eliminate from its transactions all unnecessary use of alcohol and all alcoholic preparations that are consumed as beverages.

G. M. B.

#### TO HOLDERS OF NON-BEVERAGE ALCOHOL PERMITS, FORM 737:

The Commissioner of Internal Revenue has ruled in answer to a question as to whether it is necessary for druggists who are already bonded on Form 738 for the use and sale of distilled spirits for other than beverage purposes to file new bonds, prescribed in Treasury Decision 2788, in order to dispense wines and liquors in accordance with the regulations set forth in Treasury Decision 2881, that new bonds should be filed by all persons desiring to handle wines in addition to non-beverage alcohol.

Therefore, all holders of permits on Form 737 desiring to dispense wines and liquors in addition to alcohol, in accordance with the regulations, are required to file new bonds.

# TO HOLDERS OF NON-BEVERAGE ALCOHOL PERMITS, FORM 737:

The Commissioner of Internal Revenue has instructed this office to give general publicity to the following statement of the Bureau's policy in regard to the compounding and sale of medicinal and toilet preparations and flavoring extracts:

The general abuses recently discovered in prohibition territory, of preparations manufactured with non-beverage alcohol, indicate that a change is necessary in the Bureau's policy of enforcing the regulation governing such manufacture. Greater precaution must be taken to prevent the marketing, under the guise of legitimate and necessary medicinal and toilet preparations and flavoring extracts, of preparations which do not conform to the standards fixed by regulations, and which are easily and generally diverted to beverage uses. It is not only important that the revenues should be protected in this regard, but also that manufacturers who habitually comply with the regulations and take care that their preparations are not sold as beverages, should not be discredited through the operations of the unscrupulous.

The present regulations (Treasury Decisions 2760 and 2788, copies of which are enclosed) set forth the prescribed standards for all preparations in which non-beverage alcohol may be used.

Hereafter, all manufacturers of preparations in which non-beverage alcohol is authorized to be used will be uniformly held for tax and penal liability where their products have been found to be manufactured and marketed otherwise than according to the regulations. This rule will be followed even though there is no evidence indicating bad faith or neglect on the part of the manufacturer or user of non-beverage alcohol.

Permit holders are therefore informed that all preparations manufactured by them must conform to the standards of the U. S. P. or National Formulary, or Circular 19 of the Department of Agriculture, and to the regulations of the Bureau governing the manufacture and sale of such preparations. It is essential that permit holders through constant supervision and frequent tests, assure themselves that their products are being manufactured according to regulations, and the Department will hereafter hold them accountable. The duty is also clearly upon them, under the law, not only to assure themselves that their products are being manufactured in a legal manner, but that they are not distributed in such manner as to



encourage their use as a beverage. Whenever a preparation is found upon the market which does not conform to the required standards, full tax liability and all penalties, civil and criminal, imposed by the law, will be asserted regardless of the ostensible purpose for which the preparation is made.

Manufacturers, wholesale and retail dealers will similarly be held strictly accountable whenever it is found that the preparations made or distributed by them have been made or distributed under such preventable circumstances as would have assured them, had they cared to ascertain the facts, that the preparations were to be distributed and used as beverages.

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#### THE SIXTY-SEVENTH ANNUAL MEETING OF THE AMERICAN PHARMACEUTICAL ASSOCIATION.

The week of August 25 to 30 witnessed a phenomenal gathering in New York City of those interested in the various pharmaceutical organizations in America. The banquet hall and ball room and the adjacent parlors of the Hotel Pennsylvania offered exceptional facilities for the general sessions of the Association and for the meetings of the various sections, committees and Council of the A. Ph. A. and for the concurrent meetings of the American Conference of Pharmaceutical Faculties, The National Association of Boards of Pharmacy, The National Pharmaceutical Service Association and a conference of the Committee of Revision of the U. S. Pharmacopœia. It was a very busy week for many of those in attendance, as from Monday at 9.30 A.M., when the first meeting of the National Association of Boards of Pharmacy was scheduled, until Saturday afternoon, the program, as arranged, provided for a continuous round of meetings or entertainments and meetings of special committees had to be "sandwiched" with these somehow.

The first General Session of the Association was held on Tuesday afternoon, the convention being called to order by President LaWall at 3.40 P.M. The formalities usually attending such national meetings were omitted and this was one of the few occasions when the American Pharmaceutical Association convened without an invocation to the Supreme Being for guidance and direction of the exercises and deliberations. The letter of welcome from Mayor

John F. Hylan escaped being "received and not read" when one of the members called attention to the fact that such disposition would be construed as scant courtesy. The reading of the letter elicited a round of applause.

The Presidential Address was then presented and referred to a committee of which Prof. T. J. Bradley of Boston was chairman to give due consideration to the recommendations contained and report at the subsequent meeting of the Association. The remainder of the first session was consumed in calling for reports of standing committees and in selecting the all important Committee on Nominations.

A special adjourned general session was held on Tuesday evening, devoted to the presentation for the first time of the Remington Memorial Medal. The presentation on behalf of the New York Branch of the A. Ph. A. was made by Dr. Jacob Diner, whose eloquent and sympathetic tribute to the memory of one whose influence had helped materially in shaping his own career, touched a responsive chord in many of his audience and whose reference to the services that the recipient, Dr. James H. Beal, had performed in behalf of pharmacy, was heartily applauded.

In responding, Dr. Beal read a prepared tribute to Professor Remington, expressing his personal appreciation of the character and services of this distinguished teacher, author and pharmacopœial revision leader. Prior to this function, the surviving "ex-presidents" present at the convention accompanied by the members of their families had a reunion and an informal "Italian" dinner at which it was decided that in order to arrange for the continuance of their duty as a Committee of Award of the Remington Memorial Medal, the retiring president should become automatically the chairman of the committee and the Secretary of the New York Branch should continue as the Secretary.

The reports of the Treasurer, Dr. H. M. Whelpley, and of the Secretary, Prof. W. B. Day, showed that despite the general upset conditions the Association had a successful and prosperous year. Nearly six hundred members were added to the roll. At an early session of the Council, the following distinguished scientists were elected honorary members: Professor L. Guignard, honorary president Paris School of Pharmacy; Professor M. Emile Bourquelot, president Pharmaceutical Society of Paris; Professor Eugene Collin, chemist Central Laboratory for Repression of Frauds, Paris; J. H.

Maiden, director Botanical Garden New South Wales, Sydney ; Wm. Kirby, M.Sc., president British Pharmaceutical Conference, and Sir William Glyn-Jones, secretary Pharmaceutical Society of Great Britain.

The various section meetings were well attended and there was no lack of papers or of interest in the numerous and varied topics discussed, the main difficulty being the finding of the time necessary for their proper consideration. This was evidenced, for example, in the forced curtailment of the "Symposium on the U. S. P. Revision" that had been arranged as part of the program of the Section on Education and Legislation.

As a result very largely of the efforts of Mr. Frank H. Freericks, chairman of the A. Ph. A. Advisory Committee for Soldier and Sailor Pharmacists, a War Veterans Section was organized with Dr. R. P. Fischelis as chairman.

No matter what particular interest appealed to the member in attendance, he was sure to find among the papers one or more that presented subjects that contained alike food for thought and profit. If his principal interest was in matters scientific, then the various papers presented at the three meetings of the Scientific Section gave him a surfeit. If, on the other hand, as a practical dispensing pharmacist he was interested in the problems presented by others similarly engaged, he found in the Section on Practical Pharmacy and Dispensing a clearing house for the transmission of such vocational subjects. The Section on Commercial Interest also offered an unusually well prepared list of topics and addresses all of which were of the greatest importance to the adoption of correct business methods that would assure the greatest success. The same can be said with equal earnestness as to the programs of the other sections.

The several recommendations of President LaWall all looked toward improving the service rendered by the A. Ph. A. and the making of this Association a still greater factor in furthering the welfare of humanity. The recommendation that the Code of Ethics be revised and then printed on the application blank for membership, or if that be not possible, that a copy be distributed with each such blank, so that there will be constantly in evidence our professional ideals to which each member is to subscribe, was unanimously adopted. The question of advancing the dues to \$7.50 was referred to a referendum vote of the members to be taken along with the annual election by mail.



The Committee on Research was continued with authority to co-operate with other associations planning research work along cognate lines which are based upon service to the profession as a whole or to the public which is the ultimate benefactor. Incidentally, the A. Ph. A. committee on research recommended that the award of the fund available this year be made to George D. Beal, of the University of Illinois, to carry on research on the anthraquinone-containing drugs, and this met the approval of the Council.

The recommendation of the President that laws should be framed covering and regulating the proper dispensing of medicines in hospital practice as such dispensing was equally as important as the practice of pharmacy to the public, was directed to the attention of the National Association of Boards of Pharmacy as one requiring early attention and legislation.

His recommendation that in the selection of delegates to the forthcoming pharmacopœial convention, the Association should be represented by delegates who will attend the Convention and who will be suitable for service on the new committee of revision, was a timely reminder of duty that was favorably received and adopted.

Another recommendation dealt with the subject of a pharmaceutical corps in the U. S. Army and recommended that the American Pharmaceutical Association again place itself on record as favoring the recognition of properly qualified pharmacists by elevation to commissioned rank in a corps affording an opportunity for distinctive service and that the officers of the A. Ph. A. be directed to coöperate fully with all other organizations having the same object in view. The Report of the Committee on Status of Pharmacists in Government Service dilated further upon this subject and advised a continuation of efforts with the Surgeon-General with the hope of ultimately securing the endorsement of the Medical Department of the Army and that a committee of three members be appointed to coöperate with similar committees appointed by other pharmaceutical associations to present to the Surgeon-General the need for modern pharmaceutical service in the medical department of the army and to further the aims of pharmacy in the other branches of the government service. This Committee also urged the endorsement of the bill introduced by Representative Darrow, H. R. 4760, to increase the efficiency of the Medical Department of the U. S. Navy and to improve the status and efficiency of the Hospital

Corps of the U. S. Navy. Also that the Association approve of the efforts to secure improved pharmaceutical service and recognition for pharmacy in the Public Health Service. These several recommendations of the committee and of the president harmonized and were adopted by the Association.

Another recommendation adopted in a somewhat modified form provides that the mail ballots in the future contain opposite to each candidate's name his address and vocation.

Other recommendations adopted provide for the election of an executive committee of the council and as one of the first duties of said committee the searching of the presidential addresses for the past ten years for pertinent suggestions that have been overlooked and which are of present value and importance.

The weather throughout the week was enjoyable, being free from excessive temperature, humidity or severe storms and this undoubtedly added greatly to the enjoyment of the visitors and the spirit that marked every occasion. The entertainments were varied, including vaudeville entertainment, auto ride to the Botanical Gardens and Museum in the Bronx and to other points of interest, the Alumni Luncheon, a composite function participated in by the alumni of all the schools represented with friends and relatives in attendance, a boat ride up the Hudson and then to Coney Island with a coupon ticket to many of the amusements and this topped by a shore dinner at the Balconnades in Luna Park.

The local committee spared neither effort nor expense in their endeavor to make this the greatest and most enjoyable meeting of the A. Ph. A. and their excellent arrangements for both meetings and pleasures added materially in assuring both comfort and benefit for all who were fortunate enough to attend. The sixty-seventh meeting of the American Pharmaceutical Association was certainly a memorable event in the history of American pharmacy and must have a telling effect in its future advancement.

It was determined to hold the next meeting in Washington during the first week in May and just prior to the United States Pharmacopœial Convention.

## THE STANDARDIZATION OF *PISCIDIA ERYTHRINA* (JAMAICA DOGWOOD).\*

BY PAUL S. PITTENGER, PHAR.D., AND GEORGE E. ÉWE.

Although the amount of Jamaica dogwood prescribed and used by the present-day practitioner is very small as compared with such drugs as cannabis and opium, which possess a somewhat similar but more powerful action, the drug is still used in appreciable quantities.

It is the opinion of the authors that any drug which is worthy of being used as a medicinal agent should be standardized either by chemical or biological methods.

As we were unable to find in the literature any satisfactory method of assaying Jamaica dogwood, we conducted a series of experiments with the object of developing, if possible, either a chemical or a biological method for standardizing this drug.

Since the principal end to be accomplished by the assay of a drug or its preparations is to secure a *means of measuring its therapeutic efficiency*, a chemical method fails of its purpose unless some direct and constant ratio exists between the figures obtained by the assay process and the therapeutic activity of the drug. For this reason it was necessary for us to first develop a satisfactory biologic method for measuring the therapeutic *activity* of the drug. Without a satisfactory biologic method it is impossible to determine whether or not the substance isolated by chemical means bears any relation to the activity of the drug.

We, therefore, first devoted our attention to the physiologic action.

### PHYSIOLOGIC ACTION.

The researches of Ott<sup>1</sup> and Nagle<sup>2</sup> show that Jamaica dogwood possesses a marked sedative, analgesic and hypnotic action.

Of the three actions mentioned, the hypnotic effect presented itself as the most likely means of physiologic standardization.

\* Read before the meeting of the Pennsylvania Pharmaceutical Association, Buena Vista Springs, June 26, 1919.

<sup>1</sup> Ott, Isaac: *Therapeutic Gazette*, 1883, supplement to March number, pages 12 to 17 inc.

<sup>2</sup> Nagle, A. C.: *Druggists Circular*, Feb., 1881, p. 18.



The similarity between the actions of Jamaica dogwood and cannabis suggested the possibility of employing similar methods of standardization.

A fluid extract of the drug was accordingly administered in capsules to dogs and found to produce incoördination and ataxia similar to that produced by cannabis.

The hypnotic effect of Jamaica dogwood, however, was found to be less than that of cannabis, as it required approximately 17 times as much Jamaica dogwood to produce the same degree of incoördination in dogs as that produced by cannabis.



FIG. 1. Normal Dog.

For standardization purposes the end reaction to be observed is one just sufficient to produce muscular incoördination in a dog.

The details of the method employed follow:

*Animals.*—Short-haired dogs of medium size (6 to 12 Kilos) are well adapted for this work. They show the different stages of the drug's action because of their comparative high cerebral development.

Animals for assay purposes should be selected with great care, it being necessary to pick out those that are healthy, intelligent, quiet, and which have shown by previous tests that they are easily susceptible to the action of the drug.

After several dogs have been selected, the operator, before using them for actual work, should study each animal in order to familiar-

ize himself with the behavior, peculiarities, etc., of the dog under normal conditions. The same animal may be used many times, provided that twenty-four to thirty-six hours are allowed to elapse between doses in order that the animal may *completely* recover from the effects of the previous dose.

Although the animals never appear to lose their susceptibility, it is not advisable to use a dog for more than six months, and care should be taken to allow one week to elapse between assays.

*Preparation of Experiment.*—Select and weigh several animals which have been found easily susceptible to the action of Jamaica dogwood, and withhold all food for at least twelve hours previous to the time of administration of the drug. Water should be allowed.



FIG. 2. Same dog as shown in Fig. 1, one hour after receiving a dose of active Jamaica dogwood. This figure clearly illustrates the stage of incoordination produced by Jamaica dogwood. That the dog has lost control of the hind legs and of the muscles supporting the head can be noted by the drooping of the head and hind quarters. Also note that the legs are spread apart in order to maintain balance.

*Preparation of Drug for Administration.*—Tinctures, solid, powdered, and fluid extracts, are weighed or measured directly into hard gelatin capsules. When a crude drug is to be tested a representative sample should be finely ground and then made into a fluid extract.

*Method of Administering.*—The drug is administered internally by means of a small capsule. The animal's mouth is opened by

forcing the thumb and index finger of the left hand between the jaws, neck and teeth. The capsule is then placed on the back of the tongue with the right hand and the mouth quickly closed; while still holding the mouth shut, the animal can be made to swallow the capsule immediately by slapping it on the throat.

*Actual Standardization.*—Administer to a series of three selected dogs 9/10, 10/10 and 11/10 of the standard dose of the preparation to be tested, for each kilo body weight of animal. The animals are then placed in a room where they will be undisturbed and are remote from noise and excitement; careful observation should be made and the results recorded during four or five hours.

If this preliminary test shows that the drug is either above or below standard strength other dogs are given progressively increasing or decreasing doses, as the case may be, until the smallest dose per kilo body weight is found which will produce an action just sufficiently pronounced to bring on the stage of incoördination. This is distinguished by a slight ataxia when walking and a drooping of the head and gentle swaying of the body while at rest. The relative strength of the preparation tested is then computed between the "minimum dose" and the "standard minimum dose" by simple proportion.

The personal equation plays an important part in this assay just as in cannabis, since the accuracy of the test depends largely upon the experience of the operator and his ability in determining just when the effects of the drug manifest themselves. In the hands of an experienced operator, therefore, results may be obtained which will show, with fair accuracy, the relative value of any preparation of Jamaica dogwood.

#### TENTATIVE STANDARD.

In order to determine the average amount of the drug per kilo required to produce incoördination in dogs and to set a tentative standard for assay purposes, ten different samples of fluid extract obtained from the various pharmaceutical manufacturing houses in the United States were assayed by the above method and were found to produce incoördination in dogs in the following doses:



Sample No.

1 .....	0.7	Mils per k. body weight of dog
2 .....	0.6	" " " " " " "
3 .....	0.5	" " " " " " "
4 .....	0.4	" " " " " " "
5 .....	0.7	" " " " " " "
6 .....	0.5	" " " " " " "
7 .....	0.4	" " " " " " "
8 .....	0.4	" " " " " " "
9 .....	0.5	" " " " " " "
10 .....	0.5	" " " " " " "

You will note, therefore, that the average of the above ten samples is 0.52 Mils per k. We have, therefore, adopted the following tentative standard:

"Fluid extract of Jamaica dogwood should be of such strength that it will produce incoördination in dogs in doses of 0.55 Mils per kilo body weight of animal and should not produce incoördination in doses less than 0.5 Mils per kilo, the drug being administered by capsule after fasting the animal for 12 hours.



FIG. 3. Another view of the same dog as shown in Fig. 1, one hour after receiving dose of Jamaica dogwood. This figure shows the animal when severely affected. Note that the legs are spread apart in order to maintain balance, also the drooping of the head and the bowed back.

The above experiment also shows the wide variation in the strengths of the commercial preparations on the market and proves the necessity for standardizing preparations of this drug.

## CHEMICAL INVESTIGATION.

The only physiologically active constituent which could be found credited to Jamaica dogwood in this investigation was the crystalline substance "piscidin." Piscidin is credited by Berberich<sup>3</sup> as having the formula  $C_{29}H_{24}O_8$ . Berberich also states that Edward Hart<sup>4</sup> by treating the fluid extract of the bark of Jamaica dogwood with slaked lime, obtained a crystalline substance, which he considered to be the active principle of the bark. The crystals separated on the sides and bottom of the flask, in which the experiments were conducted, after the mixture had stood for two or three days. The crystals were accompanied with a resinous substance. They were purified by recrystallization from alcohol and were finally obtained in a nearly colorless condition. After repeated crystallization from alcohol, the substance was obtained in the form of small yellowish crystals, which, under the microscope appeared to consist of four- to six-sided prisms. Hart further described the crystals as "insoluble in water, slightly soluble in cold, much more in boiling alcohol, only slightly soluble in ether and easily soluble in benzene and chloroform. It is dissolved by strong hydrochloric acid and sulphuric acid and precipitated from these solutions, apparently unchanged, by water. Fehling's solution failed to detect glucose or sucrose. The alcoholic solution is neutral to litmus. Alcoholic lead acetate solution does not produce a precipitate." Berberich found crystals of piscidin to melt at  $192^{\circ}$  C. and that they conformed to the formula  $C_{29}H_{24}O_8$  by elementary analysis. He named the substance "piscidia." Berberich repeated the experiments of Hart. He made a fluid extract from 500 Gms. of the bark by use of 78 per cent. alcohol. The extract was concentrated by distilling off the alcohol until about 100 Mils of liquid remained. This liquid was poured into a beaker containing 30 Gms. of quicklime which had previously been slaked with enough water to make a thick paste. The milk of lime and concentrated extract were intimately mixed, the mixture was allowed to stand in a warm place for one half hour, strained and the residue pressed. The liquid was then filtered. Water was added to the clear filtrate until slightly turbid. After

<sup>3</sup> Berberich, Herman: AMERICAN JOURNAL OF PHARMACY, Sept., 1898, pp. 425-427.

<sup>4</sup> Hart, Edward: *American Chem. Journ.*, 1883, p. 39, also *Therapeutic Gazette*, 1883, pp. 97, 98.

two or three days, crystals separated upon the sides and bottom of the beaker. They were accompanied by a resinous substance from which they were purified by recrystallization from alcohol. By adding water to the mother liquor a second crop of impure "piscidia" was obtained. These purified crystals possessed all of the properties assigned to "piscidia" by Hart.

We have repeated the work of Hart and Berberich with the exception of the melting point determination and elementary analysis and have obtained the same results noted by them.

A modification of the lime method of isolation of piscidin was developed in the hope that it might be applicable to the assay of fluid extract of Jamaica dogwood by chemical means. The details were as follows: 100 Mils of the fluid extract were placed in a centrifuge bottle which had been tared with 10 Gms. of U. S. P. slaked lime in it. The bottle with its contents was weighed to obtain the weight of the sample and the bottle was stoppered and allowed to stand with frequent agitation at 40–50° C. for a half hour. The bottle was then centrifuged and as much of the clear liquid as possible was removed and filtered into a tared 250 Mils Erlenmeyer. The Erlenmeyer was weighed to obtain the weight of the sample. The sample was diluted with 3½ times its weight of freshly boiled and cooled distilled water. The Erlenmeyer was then corked well and allowed to stand at room temperature for three days with occasional agitation. The crystallized piscidin was filtered off on a tared Gooch, washed with 15 per cent. alcohol and dried at 100° C. to constant weight. Some of the piscidin adhered tenaciously to the flask, so the flask was weighed to obtain the weight of the adherent piscidin, which was then added to the weight of the piscidin found in the Gooch.

Dilution of the aliquot with 3½ times its weight of water was decided upon as yielding the maximum proportion of piscidin, as shown by the following experiments on one fluid extract:

Experiment No.	Aliquot.	Water Added.	Piscidin.
1	50 Mils	50 Mils	0.182 Gm. per 100 Mils
2	" "	175 "	0.219 " " " "
3	" "	500 "	0.220 " " " "

The piscidin yielded by this process is contaminated by resinous matter. Separation of the piscidin and resin was attempted by



means of solvents but without success. Recrystallization of the piscidin from alcohol resulted in purification of the piscidin but this method is not applicable quantitatively to the small amounts obtained in an assay process.

In order to ascertain the relation of the piscidin recovered by this process to the activity of the fluid extract from which it was obtained, the amount of piscidin yielded by 100 Mils of a fluid extract was redissolved in hot alcohol, then diluted to 100 Mils with the weakest strength alcohol which would keep the piscidin in solution and this solution was then tested physiologically in comparison with the original fluid extract. In two experiments the piscidin recovered by assay represented 55 per cent. and 62.5 per cent. respectively of the activity of the fluid extracts.

Ten samples of fluid extracts representing all of the larger pharmaceutical manufacturing houses in the United States were assayed by this lime process in comparison with the physiological assay process in order to determine whether or not the piscidin content paralleled the physiologic activity. The results of these assays follow:

Sample No.	Chemical Assay.			
1 .....	0.219 per cent.	impure piscidin	0.7 Cc.	per kilo.
2 .....	0.235 per cent.	" "	0.6 Cc.	" "
3 .....	0.450 per cent.	" "	0.5 Cc.	" "
4 .....	0.460 per cent.	" "	0.4 Cc.	" "
5 .....	0.507 per cent.	" "	0.7 Cc.	" "
6 .....	0.620 per cent.	" "	0.5 Cc.	" "
7 .....	0.620 per cent.	" "	0.4 Cc.	" "
8 .....	0.650 per cent.	" "	0.4 Cc.	" "
9 .....	0.670 per cent.	" "	0.5 Cc.	" "
10 .....	0.680 per cent.	" "	0.5 Cc.	" "

These comparisons show that the piscidin content is not in direct ratio to the physiologic activity and therefore make evident the impossibility of using the lime method of isolating piscidin, as a means of chemically standardizing Jamaica dogwood preparations. We have made some experiments with the view of employing lead subacetate in place of lime but the recovered piscidin is likewise contaminated with other substances, but to what extent is not known at present and will be reported upon in a later communication to this Association.

*Conclusions.*—The result of these experiments would tend to prove, therefore, that we are without a reliable chemical means of accurately standardizing Jamaica dogwood preparations but that they can be accurately standardized by physiological means as outlined in this paper.

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## THE USE OF ANIMALS IN THE DEVELOPMENT AND STANDARDIZATION OF MEDICINAL PRODUCTS.<sup>1</sup>

BY HERBERT C. HAMILTON,

DETROIT, MICH.

“The Meyers bill, just introduced in Congress, making it a crime to vivisect the dog, carries into the open and vociferous forum of public debate a question that has disturbed the friendly relations of doctors and dog-lovers for decades.

“There are all shades and degrees of opinion on the subject, all coming at last to the prime consideration of whether it is right under any circumstances to endanger, or take the life of one living being for the sake of another.

“So many of the sound principles of modern surgery have been established by experimentation on dogs, cats, monkeys and other animals, to the very great benefit of human beings, it will be rather hard for the anti-vivisectionists to hold their ground, particularly if they are still eaters of chops from the innocent lamb and steaks from the cunning calf.”<sup>2</sup>

In searching for a logical reason for the animus against vivisection one must conclude that it is based on one or the other of two ideas: first that the use of animals in colleges and research laboratories, is unnecessary and avoidable; second, that such use of animals is needlessly cruel and inhuman.

<sup>1</sup> From the Research Laboratory, Parke Davis & Co., Detroit, Mich.

<sup>2</sup> Editorial, *The Detroit Journal*.

Regarding the first of these it should be sufficient to point out that while many of the valuable medicaments were undoubtedly discovered and their values determined by observation of their effects on humans, research men are not now so favorably placed; it is rare indeed when one can find a person willing to be the first on whom a substance which may or may not be a therapeutic agent, shall be tried. The risk is too great, for the toxicity may be greater than its medicinal value.

Regarding the second of these, while in some cases a preliminary anesthesia is not possible, in a large percentage of the cases where animals are employed for ascertaining the effect of a drug, the observation can be made much more carefully, and more accurate deductions drawn if the factor of pain be excluded entirely.

It should be noted further that the use of animals in research is always with the hope of learning facts which will be helpful in relieving pain or saving lives, either human or animal.

This cannot be said of the great destruction of animal life by hunters and trappers who wound or kill for pleasure and only incidentally for profit; a profit which is almost always personal.

It cannot be said of the slaughter of animals for food, since animal food is not essential to life.

It cannot be said of the slaughter of animals for bounty, since in many cases the losses caused by certain animals on whose head a price is set is less than those losses due to an abnormal increase in the numbers of other predatory animals which had formerly been their prey.

Another point not to be overlooked is that in some cases, notably that of using dogs, the demand for research uses rarely equals the supply of undesirables which would have been killed with no useful return, while in other cases, such as guinea pigs, rats and mice the normal supply must be constantly augmented by intensive breeding, in order to meet the demand for research and testing purposes. The use of dogs is therefore no economic loss, and the death no more painful in general than the form of death decreed by the municipality.

General statements, such as those made above, are of little value in combating the untruths and half truths of the anti-vivisectionist. In no other way than by a general investigation can the falsity and absurdity of many of their statements be established.

It has seemed best to meet the situation by a history of the de-



velopment of certain products, and the methods of testing, together with an emphasis on the value to the world, on the one hand, of an intimate knowledge of the properties of medicinal substances, and on the other hand, the benefit resulting from accurate knowledge of the life processes in health and in disease. One must start with certain premises such, for example, as these:

That some medicinal substances are valuable for relieving pain or prolonging life; that other valuable agents may be discovered or developed, substances possibly more valuable than those with which we are familiar; that most human lives are more valuable than the average animal's life. It follows, therefore, that almost any number of animals might be used in developing a remedy for tuberculosis, for example, which, in the U. S. alone, has a toll of 150,000 lives yearly.

There is still another side to the picture—the saving of animal life. Hog cholera in one year, in one state of the Union, caused a loss of nearly 3,000,000 hogs, while one hog, when hyperimmunized with the virus, will supply serum sufficient to immunize 100 hogs.

The disease of rinderpest in South Africa has been practically exterminated by following the information gained from animal experimentation. It is a disease from which hundreds of thousands of cattle died annually, but the antivivisectionist sees only the rabbits that were inoculated to study the disease and the remedial measures, while the suffering and death among millions of infected cattle is overlooked.

What is the answer? What of experiments to eliminate Texas fever in cattle, white scours in calves, chicken cholera, dog distemper? When a disease causes an economic loss and waste of valuable life, experiments are undertaken to eliminate or control the disease, whether it is human or animal life. Vivisection in its broader application therefore saves the lives of thousands of animals to one that it takes.

Antitoxin for diphtheria required the use of a large number of animals before it was perfected but its use has reduced the mortality from over 80 per cent. to under 20 per cent. of those attacked. While in some cases improved hygienic measures may be equally responsible with the remedial agent for a lowered death rate, there is, practically, no other treatment for diphtheria than the administration of antitoxin.

In preparing antitoxin by developing it in the horse's blood, a certain number of horses are valueless for this purpose because the immune bodies will not develop or will acquire only a nominal potency. How is this to be determined? On your child or mine? Or is it more humane to standardize the serum on guinea pigs and by this means eliminate antitoxin of low potency which is indistinguishable from a potent sample by any known test except that on the living animal or human being?

Recently in the daily press, we read of the men who, in the interests of the army as a whole, served as a means of demonstrating whether or not trench fever is transmissible by "cooties." While this disease may not be regarded in the same category as some, during the war it involved discomfort and possible death to many a soldier. This method of study was necessary because it is impossible by animal experiment to demonstrate the correctness of the theory.

The world proclaims as a hero the physician who risks his life to verify certain facts, such as the transmissibility of yellow fever and malaria by the bite of the mosquito. If it were possible to substitute the life of a dog or a horse for that of the man with equal benefit to the world, would it be difficult to choose? The average person would say that the physician was the more valuable to the community and the world.

The natives of Africa were able to make their weapons more effective by dipping the arrow points into a poison prepared from certain seeds, finely ground, and partially extracted. Careful study of this poison on animals revealed the fact that it has a peculiar effect on the heart, causing, in sublethal doses, a slowing and strengthening of the heart beat.

In certain cardiac diseases, where the pulse is weak and rapid, it is logical to use strophanthus, the arrow poison, to counteract the abnormal condition. No statistics could be collected to show the value of this remedial agent, discovered by the hunter and developed by the pharmacologist, the vivisector, but its constant use indicates its importance. To-day, although its place is secure as one of the most valuable of the heart tonics, strophanthus still exacts a certain toll of lives? Why? Because the physician prefers that some almost worthless frogs should die than that he should use an overdose of this powerful drug.

One of the most valuable phases of animal experimentation is the elimination of harmful and of valueless drugs, giving the physician greater assurance of obtaining the desired results from administration of remedies. From this also has resulted the substitution of the pure principles for the crude drugs and nauseous extracts previously used.

It is a common occurrence to find on the market strophanthus seed, as low in activity as one fourth that of the adopted standard and, on the other hand, two or three times as active as this standard. An under dose as, for example, a dose from a sub-standard preparation, might be harmless, but if a life were hanging by a thread and required a dose of an active heart stimulant, either a highly potent or a worthless sample would be equally fatal. In the one case, the worthless sample would not stimulate the heart muscles to the necessary activity. In the other, an extract of an exceptionally potent lot of drug would poison the heart by overstimulation and just as surely cause death.

Ergot is another illustration of this. It has been used for centuries in aiding childbirth and arresting hemorrhage, but has suffered often from the fact that it is uncertain in its action, some extracts being apparently devoid of any action on the uterus. With my memory, a German chemist put on the market the supposedly active principle called clavin. This substance might be tested in two ways, either in cases of labor on human subjects, or by a few careful tests on anesthetized animals. Two or three tests by the latter method were sufficient to show that clavin was quite inert.

Further chemical, combined with pharmacological, investigations established the fact that ergot owes its therapeutic value to three active principles each of which has its well-marked effect and each of which is equally essential to the complete action of the drug. Without animal experiments carried out in connection with the chemical investigations the composition of ergot and its rational use would still be uncertain. Even with our present knowledge of its composition we are still unable to standardize extracts of ergot except by a physiological test. The usual test applied, however, does not involve death, anesthesia or even suffering except the prick of the hypodermic needle.

The uncertain effects of extracts of *cannabis indica*, before physiological experiments established the fact that this is due to



variable quality, almost discredited the drug as a therapeutic agent. The question may logically be asked why chemical tests should not be applied to standardize medicinal substances. In reply to this, it may be sufficient to say that pharmacologic standardization (vivisection in one of its broader aspects) is applied only where the active agent is of such a character that chemical tests cannot be applied. It is a more expensive and a less accurate means of standardization and in no case will be retained after an accurate chemical test has been developed.

Pellagra, scurvy, beri beri and some other less well-marked diseases of undernourishment, have to a large extent, been of necessity studied on human subjects. In that way observers have learned that certain foods are essential but that certain forms of food seem deficient in nourishment. In one historic instance a group of Dr. Goldberger's assistants—16 in all, of whom 13 were physicians—voluntarily submitted themselves to experiments in order to demonstrate whether the symptoms of pellagra could be reproduced by any method of infection. The materials used were blood, nasopharyngeal secretions, epidermal scales from skin lesions, urine and feces. These were administered by injections, by application to the mucosa of nose and pharynx, and by mouth. The evidence while negative led to the conclusion that the disease is one due to faulty diet. Assuming that a corrected diet will eliminate one of the worst scourges of the South, who will deny that these physiological experiments were worth while? On the same principle and even with greater humaneness, the use of animals is to be commended wherever such use is possible.

The development of vitamins is another triumph in which physiological studies have suggested the introduction of a valuable therapeutic agent. By experiments on pigeons, rats and guinea pigs, it is possible to demonstrate a life process which could be only inferred from observations on humans, to prove that certain foods are deficient although supposedly containing all the essential constituents. In scurvy, the lacking factor is found in certain fresh foods or in lemon or lime juice; in pellagra, it is apparently in part the substance in the shell or germ of the corn which is removed in milling; in beri beri, it is a loss of the substance removed in polishing rice, or in certain conditions occurring when foods are prepared.

In humans, the disease is slowly developed and responds only

slowly to treatment since it is usually complicated by accompanying pathological processes not directly connected with the disease. In pigeons, on the other hand, the condition of polyneuritis can be developed in a remarkably short time by a diet consisting largely of polished rice, while the recovery from this condition takes place in only a few hours when an extract of the polishings of the rice or, better still, an extract of yeast is administered. The chemical characteristics of these various therapeutic agents are as indefinite as the exact status each has in nutrition, but the deficiency of each of them in the diet can now be recognized and remedial agents suggested, based on the experiments conducted by a number of prominent physiologists as Funk, Eijkman, Veddar, Hopkins, Goldberger and many others. The possible value of this work in recognizing and overcoming disease due to nutritional deficiencies is immeasurable.

Koller, an ophthalmologist of Vienna, in 1884 tested the anesthetizing properties of cocaine on guinea pigs, rabbits and dogs. After noting that in these animals the eye could be touched or scratched without pain after a 2 per cent. solution had been dropped into it, he tried the same solution on man and thus was introduced into medicine a new method of relieving pain and permitting of operations, previously unendurable.

Cocaine is an exceedingly valuable local anesthetic, but it is highly toxic and has besides a habit-forming action which greatly restricts its use. As a result of a careful chemical study of its composition and structure combined with pharmacological experiments on animals, it has become possible entirely to eliminate this drug as a local anesthetic substituting a substance almost equally efficient but at the same time much less toxic and with no habit-forming effects. This in itself would justify the practice of vivisection.

In many surgical operations, profuse bleeding is almost unavoidable, even with the utmost precautions. Further, there are many individuals whose blood is very slow in coagulating and with whom an operation is regarded as almost surely fatal. By the aid of animal experimentation and from the blood and tissues of other animals, substances have been produced which when introduced into the circulating blood shorten its coagulation time so greatly that the danger from excessive hemorrhage has been largely eliminated even in those cases known as hemophiliacs.

Without vivisection such results could scarcely have been obtained. The dog, the horse, the cow and the goat contribute to this valuable therapeutic agent. The part taken by the dog is that of test animal to determine whether the active agents are present, since no known chemical test will show whether they are present in an active form. The dog is, therefore, no less essential in the cycle of operations than the other animals employed. There is no apparent reason why the dog, especially the stray, which spreads disease, contracts and transmits rabies, kills sheep and is rarely useful, should be protected, while an open season exists for deer, quail and trout, and there is no closed season for many animals more deserving of protection.

The animals mostly used in pharmacologic experiments—vivisection, if you please to call it that—are the frog, mouse, rat, guinea pig, rabbit, dog, cat and monkey. Of these, the frog owes its value to the fact that being a cold-blooded animal, its isolated tissues survive a considerable time and can therefore be used, for example, for the study of muscular contraction and the function of the nerves. The guinea pig, rat, mouse and rabbit are chiefly of value for inoculation experiments; while the cat, dog and monkey are useful particularly for experiments on the brain, central nervous system and circulatory system.

The dog is especially valuable in nutrition and digestion experiments because of its diet, which is as omnivorous as that of man. For many purposes no other animal can be used on account of the size of the organs and the convenience of handling. For blood pressure experiments in studying the heart tonics of the digitalis series, standardizing extracts of the pituitary and suprarenal glands, testing the efficiency of hemostatics and blood-coagulating agents, standardizing hypnotics, such as cannabis indica, chloral, chloretone and similar substances, no other animal is so well adapted and from no other animal can the results be transferred directly, almost without alteration, to man.

Where pain would accompany the experiment and when this point is not the subject of the experiment, a preliminary anesthesia with chloretone is usually applied. This general anesthetic can be given internally by mouth and is often so used. Complete anesthesia, recognized by the absence of reflex when the pupil is touched, results in a half hour. Anesthesia remains complete, when the proper



dose is used, until death, the animal being killed at the end of the experiment by a lethal dose of digitalis.

There are certain historical cases where animal experimentation did not precede human use, as for example, Sir Robert Christianson, who almost died from eating Calabar bean from which physostigmine comes; Koeppe, who tried the effects of digitoxin on himself with like result. Chloroform and prussic acid were also investigated with equally unpleasant results. In some cases deaths have occurred, particularly in cases of infectious diseases.

Animal experiments were used to explain caisson disease and suggest means for its prevention and remedy, animals being subjected to air pressure and the pressure applied and released under varying conditions. Such experiments have also made possible the surgical operations which have done so much to relieve pain and prolong life, the human being having the benefit of experience and skill gained by operations on animals.

While physiological experimentation and the standardization of drugs requires the use of all the animals mentioned, the dog is more widely used and is almost beyond replacement. Everyone, almost without exception, regards the dog as a highly intelligent animal, a fit companion for man. There are few dogs used in research laboratories that would have the appeal of Mark Twain's "Tale of a Dog" or that would be welcomed by any but the small boy. The class of dogs used in experiments, picked up by the dog-catcher and not redeemed, is almost without exception friendless. Even the antivivisectionist would at most feel only pity for it and with proper recognition of the use to which it is put would probably realize that in a remarkably few cases is any cruelty involved in using it as a test animal.

Most people will agree with Darwin in saying that "cruelty to the lower animals is worthy of detestation and contempt." But what is cruelty? The transportation and preparation of animals for food, the method of slaughter, hunting, fishing, trapping, are often cruel to an extreme. But they are not condemned. More actual cruelty is probably practiced in this way in a season than occurs in all the research laboratories in the world, in a year. Can vivisection be condemned and sport exonerated?

The advancement of knowledge, the mitigation of misery and the prevention of disease are surely infinitely higher and nobler

motives for infliction of pain, when pain is actually inflicted, than merely healthful exercise and transient enjoyment.

Is it logical, therefore, to attempt legislation to limit and restrict a form of research so valuable to mankind?

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## NOTES ON THE ASSAY OF HYPOCHLORITE SOLUTIONS.<sup>1</sup>

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Our attention was recently called by Dr. J. W. Sturmer to a difficulty in the assay of a sample of Dakin's solution, in which, after obtaining the end reaction the blue color returned and addition of volumetric solution had to be made repeatedly until a permanent end reaction was obtained.

The Dakin's solution in question was made by passing 4.8 Gms. (or about 1,600 Cc.) of chlorine gas into a solution containing 14.1 Gms. of anhydrous sodium carbonate (or the equivalent of monohydrate or decahydrate) per liter. Should the preparation be too strong it is diluted with a solution containing 1.4 per cent. of anhydrous sodium carbonate.

The chemical reaction involved is



from which can be calculated that 4.8 Gms. of chlorine will require 14.332 Gms. anhydrous sodium carbonate and will yield 5.004 Gms. sodium hypochlorite and also that 14.1 Gms. anhydrous sodium carbonate will require 4.717 Gms. chlorine and yield 4.954 Gms. sodium hypochlorite.

The directions for the assay of the solution are as follows: Measure 10 Cc. of Dakin's solution into a beaker or Erlenmeyer flask containing 50 Cc. of water, add 5 Cc. of a 10 per cent. potassium (or sodium) iodide solution and 2 Cc. of glacial acetic acid. Run in decinormal sodium thiosulphate solution until decolorization is complete, using starch solution as indicator.

<sup>1</sup> Read at the annual meeting of the Pennsylvania Pharmaceutical Association, Buena Vista, June, 1919.

In titrating the Dakin's solution by following the above directions the permanent discharge of the blue color required the repeated addition of sodium thiosulphate and the sum total of the volumetric solution agreed very closely with that required when the 2 Cc. of glacial acetic acid were replaced by 10 Cc. sulphuric acid (10 per cent.) or 10 Cc. hydrochloric acid (5 per cent.). In the latter cases, titration was complete with the first decolorization.

By omitting the water used for dilution, it was found that 2 Cc., or even 1.5 Cc., glacial acetic acid gave a definite end reaction, the results agreeing with those obtainable with dilute sulphuric acid. While the neutralizing power of 2 Cc. of glacial acetic acid is considerably greater than that of 10 Cc. of dilute sulphuric acid (10 per cent.) or 10 Cc. hydrochloric acid (5 per cent.), dilution of the latter does not affect its action, whilst dilution of the acetic acid considerably retards its action. To illustrate—10 Cc. hydrochloric acid (5 per cent.) (equal to 0.8 Cc. glacial acetic acid) or 10 Cc. sulphuric acid (10 per cent.) (equal to 1.2 Cc. glacial acetic acid) will give a permanent end reaction, even if diluted with 50 Cc. of water. 2 Cc. glacial acetic acid (equal to 24 Cc. hydrochloric acid 5 per cent. or 16 Cc. sulphuric acid 10 per cent.) will not give a permanent end reaction unless the 50 Cc. of water be omitted.

The Eighth Revision of the U. S. P. directed the use of 10 Cc. of hydrochloric acid in the assay of Labarraque's solution, while in the Ninth Revision, 5 mls of acetic acid are directed; the substitution of acetic for hydrochloric acid in the assay suggested the possible indefiniteness of the end reaction as noticed in the Dakin's solution.

In titrations made with a deteriorated sample of Labarraque's solution (1 per cent. available chlorine), by the U. S. P. process, several additions of sodium thiosulphate volumetric solution were necessary for a permanent end reaction, but if the quantity of acetic acid was increased to 10 mls the first decolorization was permanent and corresponded to that obtained with diluted hydrochloric acid or dilute sulphuric acid.

The results of the experiments warrant the following suggestions—(1) That the prepared test be allowed to stand one hour before titrating; (2) to increase the quantity of glacial acetic acid to 3 Cc. for immediate titration; or (3) to replace the acetic acid by a diluted hydrochloric or sulphuric acid.



THE U. S. P. TEST FOR METHYL ALCOHOL IN ETHYL ALCOHOL.<sup>1</sup>

BY JOSEPH W. EHMAN, PH.G.,

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The U. S. P. test for methyl alcohol in ethyl alcohol having failed to give satisfactory results in the hands of some workers the writer has made a series of experiments to determine the cause or causes of the variable results which have come under his notice.

The fuchsin-sulphurous acid T. S. of the U. S. P. is made by dissolving sodium bisulphite and basic fuchsin in water and adding hydrochloric acid, forming a practically colorless solution.

The test for methyl alcohol is made as follows:

The alcohol is diluted to 10 per cent. by volume, 5 Mils of this are mixed with 2 Mils of 3 per cent. potassium permanganate and 0.3 Mil of sulphuric acid; after five minutes the precipitated manganese dioxide is dissolved by adding sulphurous acid. Then 1 Mil of sulphuric acid and 5 Mils of the fuchsin T. S. "After standing for ten minutes a colorless liquid results" (U. S. P.).

The difficulty has been that when this test was applied to 5 Mils of pure 10 per cent. ethyl alcohol a positive reaction (a violet color) appeared which remained for a long time. It is not considered necessary to describe all of the following experiments in detail, as a summary will be sufficient for the purposes of this paper.

Ordinary U. S. P. ethyl alcohol, deodorized alcohol and alcohol purified by the U. S. P. process for use in making alcoholic potassium hydroxide V. S. were tested with the fuchsin reagent and all gave a positive reaction for methyl alcohol. In all other respects these met the requirements of the U. S. P.

Several samples of fuchsin from different sources were subjected to the U. S. P. tests, but while there was a slight difference in the color given by some on the addition of hydrochloric acid, and one did not decolorize so readily with sulphurous acid, they all gave the same reaction in the test for methyl alcohol.

Elvove recommends cooling the solution after the final addition of sulphuric acid and before the addition of the fuchsin reagent. A

<sup>1</sup> Read before the forty-second annual meeting of the Pennsylvania Pharmaceutical Association, June 26, 1919.

few observations were made upon the influence of the rise in temperature caused by the addition of concentrated sulphuric acid, the solution being cooled to room temperature after each addition of the acid, but the only difference noted was that when cooled the color reaction was somewhat retarded, the final color being the same, and no more attention was paid to the effect of temperature at the time.

Varying the quantity of permanganate solution and the time of oxidation had no noticeable effect upon the final color.

The usual result of the test for methyl alcohol (when applied to ethyl alcohol) was a violet color, appearing more quickly at some times than at others. But one day in making comparisons an immediate bright red was obtained which later faded to yellow, while two days previously the same solutions and reagents produced, more slowly, a violet color. On the first of these two days the temperature was abnormally high and on the last it was lower than usual. The temperature of the laboratory was nearly always above 25° C., so the indications were that these experiments had been made at too high temperatures.

Cooling the solution to 25° C. after the final addition of the acid was again found to be insufficient; cooling after each addition of the acid produced a pale violet color in about 10 minutes, which did not fade when the laboratory temperature was 27°–28° C. When the 10 per cent. ethyl alcohol was cooled to 25° C. before beginning the addition of reagents and cooled immediately after each addition of sulphuric acid and kept at 25° during the oxidation the final result was a negative test. Ethyl alcohol containing 0.25 per cent. methyl alcohol gave a positive test when made at the same time and under the same conditions, but not necessarily within ten minutes. The time required will be referred to later.

Experiments were made in which a more dilute sulphuric acid was used, thus avoiding a great increase in temperature and allowing quicker cooling, but the results were not satisfactory because the red color first produced by the fuchsin T. S. required considerable time to fade. When concentrated acid was used and the solution kept much below 25° a pale red color was produced which in ten to thirty minutes faded to pale yellow in the absence of methyl alcohol, but in the presence of methyl alcohol a violet tint appeared after the red had faded. If the solution is kept at too low a temperature the results are not satisfactory, as the fading of the red color requires too much time.

If the solutions are cooled and kept cool ( $24^{\circ}$ – $25^{\circ}$  C.) during the test a positive color reaction is obtained provided the methyl alcohol content is about 1 per cent. or higher; but if as low as 0.25–0.5 per cent. the appearance of the color may require from fifteen to thirty minutes, depending upon the kind of light under which it is viewed. With small quantities of methyl alcohol the appearance of the test may indicate a negative reaction even after fifteen to twenty minutes, if viewed by daylight. This is due to a mixture of pale tints which neutralize each other. The final color resulting when ethyl alcohol is tested is a pale yellow, but if methyl alcohol is present the pale violet tint which would otherwise appear is masked by the yellow and the solution appears to be colorless when viewed transversely by daylight, but, viewed vertically, with the light from above, it gradually changes to pale greenish and finally to pale blue or violet. When the same test is observed under artificial (yellow) light the contrast is striking; the source of light may be the ordinary "Mazda" or the carbon filament electric bulb, the open-flame gas burner or even the incandescent-mantle gas light. Viewed directly from above under either of these lights, against a white background, the first indication of the presence of methyl alcohol is a faint salmon-pink color which changes to violet-pink then cherry-red; by reflected artificial light the color is a rather pale violet; the pink to violet may be pale but distinct before any color is perceptible by daylight. These colors relate to small quantities of methyl alcohol (0.25–0.5 per cent.) and require ten to fifteen minutes. With larger quantities of methyl alcohol (1 per cent. or more) the question of light is not so important, the first color being violet and changing to purplish red in a few minutes by either light. Blank tests made on pure 10 per cent. ethyl alcohol may produce at first a pale pink or even a faint violet by artificial light, but if the temperature has been properly controlled these fade to pale yellow in ten to fifteen minutes.

The above figures are approximate, no attempt having been made to determine the exact range of temperature, but the best results were obtained at  $23^{\circ}$ – $25^{\circ}$  C. The time required for the appearance of a decided color reaction depends, of course, upon the amount of methyl alcohol present.

Sodium bisulphite is likely to be met with which has a yellowish color and the fuchsin reagent in which it is used may be sufficiently



yellow to make the final test somewhat obscure. A pure sodium sulphite was substituted and the following formula for fuchsin-sulphurous acid T. S. was found to be more satisfactory.<sup>2</sup>

Dissolve .500 Gm. fuchsin in 300 Mils warm water; cool and add 11.2 Gm. sodium sulphite (90 per cent.) dissolved in 200 Mils of water, then add 20 Mils of hydrochloric acid. The fuchsin and sulphurous acid are present in the same amounts as in the official T. S. It has been found best to allow the fresh solution to stand for a few hours before use as it may be temporarily yellow.

It is recommended that the test be carried out as follows:

In the first of two test tubes place 5 Mils of pure 10 per cent. ethyl alcohol and in the second 5 Mils of the alcohol to be tested, which has been previously diluted to 10 per cent.; cool or warm them, as may be necessary, to 25° C. by immersing in water of that temperature for several minutes. Add each reagent to the contents of both test tubes before proceeding further with either one in order to have the conditions in both as nearly alike as possible; cool both quickly to 25° C. after each addition of sulphuric acid and keep them at that temperature throughout the test. If the blank gives a bright red color at once which does not fade in ten minutes, or if a faint pink or violet appears which does not fade in ten minutes, repeat the test with both and vary the temperature. If the blank is violet after ten minutes too high a temperature is indicated; if a bright red color persists, too low a temperature. It is much more simple and quick to make a control test as above than to keep a very exact control of the temperature. In the absence of methyl alcohol no pink or violet color appears within half an hour under artificial (yellow) light, nor a pale greenish, blue or violet in one hour by daylight, the solution being pale yellow or colorless. When much methyl alcohol is present the solution will become violet at once, changing to purplish red.

CHEMICAL LABORATORY OF THE  
 PHILADELPHIA COLLEGE OF PHARMACY,  
 June, 1919.

<sup>2</sup> Elias Elvove, "Notes on the Detection of Small Amounts of Methyl Alcohol," *Jour. of Ind. and Eng. Chemistry*, March, 1917, p. 295.

A CHEMICAL TEST TO DISTINGUISH BETWEEN  
CAFFEINE AND THEOBROMINE.<sup>1</sup>

BY FREEMAN P. STROUP, PH.M.

Careful study of the properties of caffeine and theobromine has shown that structurally they are, doubtless, very much alike, the chief difference being that in the former a methyl group replaces a hydrogen atom of the latter, resulting in the molecule of the former containing one carbon atom and two hydrogen atoms more than the latter. Otherwise the arrangement of the atoms in the molecule appears to be the same in both. This being the case, the pursuit of any logical plan of testing offered no inducements, and it was decided to go at the task in a purely empirical manner.

Recalling the fact that potassium dichromate and concentrated sulphuric acid properly used produce some striking color effects with certain alkaloids, strychnine in particular, it was decided to try this combination first. The results were both surprising and gratifying. Various proportions of the salt and acid, and various techniques were tried, but the best results were obtained by carrying out the test as follows:

**THE REAGENT.**—A solution of potassium dichromate approximately one part by weight in concentrated sulphuric acid twenty parts by volume. It may be made by dissolving 50 milligrams of the salt in 1 mil of the acid, or 3 grains of the salt in 1 fluidrachm of the acid.

**THE TEST: *Technique A.***—Place on a white porcelain surface a small quantity of the alkaloid to be tested (what would lie on the tip of a small knife blade will be sufficient), spread it out to cover a space about 1 centimeter ( $\frac{2}{5}$  inch) in diameter, and put two drops of the reagent in the center of the mass. With caffeine the yellow color of the reagent is almost immediately changed to a bright bluish-green. With theobromine the yellow color is first changed to a dark purplish, which gradually changes to a purplish-green, later an olive-green, and finally to the same bluish-green that is given by caffeine.

***Technique B.***—Transfer 5 or 6 drops of the reagent to a white porcelain surface, spreading the liquid to form a spot about 2 cen-

<sup>1</sup> Presented at the annual meeting of the Pennsylvania Pharmaceutical Association, Buena Vista, Pa., June, 1919.

timeters ( $\frac{4}{5}$  inch) in diameter, and drop into the center of it a portion of the alkaloid about the size of a grain of wheat. With caffeine the most of it goes into solution promptly, for a moment or two a dark-colored zone surrounds the mass of alkaloid, but in about five seconds this changes to a bright bluish-green, spreading quite rapidly until the greater part of the yellow color of the reagent is changed to green. With theobromine solution takes place much more slowly, a dark-colored zone forms almost immediately, gradually widening until the most of the yellow color of the reagent is changed to a purplish-green, then to an olive-green and finally to bright green.

It will be noticed that in both ways of applying the test the time required for the production of the light green color is very much less with caffeine than with theobromine. This is probably due in large measure to the more ready solubility of the first-named alkaloid in the acid of the reagent.

When used in conjunction with the physical tests for these two substances, given in the dispensatories and other literature, this chemical test should make the differentiation between them a simple and certain matter.

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## PHARMACY AS A HOBBY AS WELL AS AN INTEREST.<sup>1</sup>

BY CHARLES H. LA WALL, PH.M.,

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When Bryant said "To him who in the love of nature holds communion with her visible forms she speaks a various language," he uttered a truth which has many applications; not the least of which is pharmacy.

Substituting the word pharmacy for the word nature in the foregoing quotation, gives a clue to the real reason why pharmacy holds its own in spite of commercialism and other handicaps.

There are various motives which impel a man to choose a profession. One, and probably the strongest one, is self-interest. This frequently changes in later life to a realization of opportunity for service and a desire to be helpful to one's fellow-man; motives, which, as a rule, have no place in the make-up of a young man.

<sup>1</sup> Presented at the annual meeting of the Pennsylvania Pharmaceutical Association, Buena Vista, Pa., June, 1919.



By far the strongest and most valuable motive, from the standpoint of the development and progress of any profession, is the one which has to do with the desire for mental development through the acquisition of knowledge.

The answer to the eternal "Why?" has been sought by individuals in all ages and out of this quest has arisen all that we prize in the shape of knowledge. Those who have contributed most largely to the progress of the past are not necessarily the ones who stand out like beacon lights as having enunciated important axioms, or laws, or discovered valuable elements, but the real credit belongs to the silent, patient, plodding workers, who investigate from sheer love of the work and who, little caring whether results have any practical value at the time, store up the material which genius later arranges into that classified coherence which men call Science.

Much of the pioneer work of this kind in chemistry and medicine has been done by pharmacists, whose successors too frequently see themselves frowned upon and discredited by members of both of the sister professions which have been founded and developed through her help.

Much has been written regarding these matters in order to bring pharmacists to a realization of their neglected opportunities. It is doubtful whether any effect has been, or could be, produced in changing the habits of work and of thought of older pharmacists. It is the younger members of the profession in whom the hope of advancement lies and the responsibility for their guidance is largely in the hands of the colleges, for there no longer exists the preceptor of by-gone days who guided the neophyte for a period of three years or more. His disappearance is keenly missed.

One who has his mind so set upon the commercial side of pharmacy as to be oblivious to its history, tradition and possibilities, is not to be swayed, nor perhaps even interested in the following, but it is hoped that it will be read by some of the younger generation and that some will be stimulated thereby to select and encourage such applicants for entrance into pharmacy as betray an interest in the romance and sentiment which are so closely interwoven in its scientific possibilities.

Let us take a brief survey of some of the substances of which medicines are made, with which the pharmacist has more or less frequently to handle.

The tales of adventure, of conquest, of romance, the experiences

of intrepid explorers, of pioneers and colonizers of lands newly discovered, of fortunes gained and lost, of mystery, superstition and witchcraft, of comedy and of tragedy, which are associated with some of even our commonest drugs, would make even a reader who read only for entertainment and stimulation, not for improvement, forsake the most daring writers of fiction.

From the Babylonians, that ancient race of mystery and culture, come the names of some of our most important metals, names by them on account of their fancied association with, or influence derived from, the better known heavenly bodies. Most of these names are only encountered in little used synonyms; as *crocus Martis* for ferric oxide; *sassharum Saturni* for sugar of lead; lunar caustic for silver nitrate; but it is interesting to note that the planetary name Mercury still persists for this most commonly used name of one of our metals, whose compounds are of medicinal importance and value.

Passing along the shelves of any pharmacy and picking out at random from the titles those of more than passing interest, we find one of our best known cosmetic creams, the ointment of rosewater or cold cream, credited as to its origin, to Galen, one of the fathers of pharmacy, who lived at about the beginning of the Christian Era, and for centuries this preparation was called *ceratum Galeni*.

Galen's influence upon pharmacy and medicine was greater than that of any other single human being who ever lived, or probably will live. His teachings held almost undisputed sway for more than fifteen hundred years, during part of which time, in some parts of the world, pharmacists and physicians were required to pledge themselves to follow his teachings and practice blindly and implicitly.

The names of many others of the preparations and substances used in pharmacy are of interest in their origin and development. *Hiera picra* means "sacred bitters," evidencing the esteem in which it was once held. *Sal ammoniac* derives its name from the fact that it was found in the sands of the Lybian Desert near the temple of Jupiter Ammon, resulting from the decomposition of camel urine due to the many caravans which stopped at that point. The influence of the Arabians upon pharmacy may be traced through the nomenclature; the words beginning with *al* (and sometimes *el*) being of Arabic origin, as alkali, elixir, alcohol, etc. In the case of the name alcohol the Arabic word means finely divided and was first applied to easily diffusible volatile liquids and finally to the specific substance alcohol.



It is of interest to note that this earlier and original meaning persists in the title "alcoholized iron," a form of metallic iron resembling reduced iron, but prepared by mechanical and not by chemical methods; the word "alcoholized" in this title signifying simply, finely divided, and having no reference whatever to alcohol, as is mistakenly supposed by many who have handled and used it.

The Latin title *spiritus vini rectificatus*, so long used for alcohol, reminds us of the original source of the alcohol of commerce, which was wine. This title, still found on older shop furniture, is not correct as applied to modern alcohol, which is the produce of fermentation of any saccharine material. That the abbreviation S. V. R. which was frequently employed in former times to designate this substance in hastily written prescriptions, is no longer intelligible, was lately instanced by a student who rendered it, in answer to an examination question, "Service very rapid."

Phosphorus (light-bearer) corrupted into foxfire by country people who see the gleam of phosphorescent decayed wood in a forest on a dark night; antimony (against monks); vitriol (glass like); sal aeratus (gas- or air-producing salt); each of these names alone might furnish material for an article, yet we use them without a thought of their underlying interest and origin.

Of the many synonyms of compound tincture of benzoin, which have accumulated during the centuries in which it was esteemed and used as a vulnerary, Jesuits' drops and Friars' balsam give it a religious association which is distinctly different from the martial thoughts called up by balsam of Maltha, although the Knights of Malta probably used it in the Crusades.

Our common substance sodium sulphate, now almost exclusively used in veterinary practice, was discovered in the waters of a European spring by Glauber, a German chemist, whose name appears in its synonym (Glauber's salt) and so highly was it esteemed as a remedy in the early years of its use that it was called "sal mirabile," or the admirable salt.

Red oxide of mercury (erroneously called red precipitate, for it is not made by precipitation) conjures up visions of Priestley working in his home in the Susquehanna Valley with the crude apparatus which he fashioned from glass bottles, kitchen utensils and an old gun barrel, for it was from this substance that oxygen was first evolved by him in amounts sufficient to identify it and study its properties.



Morphine brings to mind Serturner in his little apothecary shop in Eimbeck, Germany, competing, all unawares, with the French pharmacist Derosne for the honor of discovering the first alkaloid morphine (called then vegetable alkali).

When we come to the drugs of vegetable origin we find the greatest opportunity for memory and imagination to run riot as our eyes glance over the list. Opium bringing to mind early morning in dew-kissed fields of snow-white blooms and nodding fruits and of the care that must be taken in incising the outer surface of the capule so as not to lose the drop or two of milky juice that subsequently hardens and becomes what was formerly called meconium, now the opium of medicine and pharmacy. Conium, with its mousy odor, reminding us of the death of Socrates and through that association of ideas of Plato and the other Greek philosophers who enriched our minds and thoughts for all time with their speculations and maxims.

Myrrh, frankincense, cinnamon, cloves, nutmegs and their like, what thoughts of caravans plodding across sandy wastes; of odorous Eastern isles; of fleets of galleys and later of sailing ships, are brought to memory. The trade in spices and precious gums and balsams has been responsible for the establishment of kingdoms and republics of olden times of commercial rivalries more fiercely waged than any of modern times, resulting in the overthrow of dynasties and in repeated changes in the world's map, and this chapter alone is well worth perusal. How many who handle and use nutmegs, with their white powdery coating of chalk, know that this is now a meaningless custom dating from the days when the Dutch, who controlled the spice islands, dipped the nutmegs in milk of lime to prevent their germination, thus assuring a monopoly in their growth and sale for centuries.

It is to the new world that we must turn, however, for some of our most interesting drug histories. Cinchona, a drug of mysterious origin as to the discovery of its properties, for it is not to-day, nor has it ever been, used as a medicine by the natives of the Andean slopes where it is indigenous.

Ipecac, used as a secret remedy for dysentery by a celebrated European physician, whose successes were so great that a French monarch paid him a handsome sum to divulge the name and origin of the remedy.

Sarsaparilla, once vaunted to the skies as a remedy in many

chronic affections, masquerading for years under false colors as to its real value; for both its alleged therapeutic properties and its flavor were due to other drugs used in its combinations; now almost entirely discredited as a remedy of any value.

Hydrastis and sanguinaria, the yellow and red "puccoon" of the aboriginal American, who used them for pigments as well as for their medicinal value.

Boneset, tansy, pennyroyal, horehound, all of these conjure up visions of old-fashioned attics with bunches of dried herbs suspended from the rafters.

Fucus and chondrus bring with them the tang of the sea and of rock-bound weed-strewn coasts, where surging billows want the mariner that Poseidon never sleeps.

With these thoughts singing through one's mind, how can anyone say that pharmacy is decadent, or that it holds no interest for its devotee. There is much and great work yet to be done and discoveries will yet be made bringing to their authors fame and possibly fortune.

Each day's work becomes a miracle to him who looks with seeing eyes into the graduate or mortar, test-tube or flask, and to him who with interested mind draws near to nature's manifestations of her innumerable laws, immutable and sometimes inexplicable. Who is there that has not time to add his quota to the knowledge of his time and of his calling, be it ever so little. Each day some new fact may be learned and recorded; untrodden paths of experimentation lie waiting for generations of pharmacists yet to come. Shall we now pass them by and leave to those of the future our responsibilities in the present?

The studying of colloids, of the sera and vaccines with their fascinating theories and illimitable possibilities; these are subjects in which any pharmacist of the present generation may be as well posted as the foremost savant of the time, for they are of such recent development that one may easily start at the beginning.

If pharmacy sleeps and is not yet aroused to her possibilities, it is time for her to awake, and this awakening will come, when it does come, through a realization of the infinitely interesting possibilities for development along lines of combined scientific and practical value. Let us all join hands in building more strongly for the future, by inculcating in our younger workers that abiding love for and interest in pharmacy which shall outlast all ephemeral consid-

erations of expediency and commercialism, except as absolute necessities. Pharmacy as a hobby adds to the happiness of the individual and can be turned to profit.

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## ON ADVERTISING.

BY JOSEPH JACOBS,

ATLANTA, GA.

The article by Dr. Jacob Diner on advertising in the July number of the *AMERICAN JOURNAL OF PHARMACY*, has much to commend it. It shows a real and practical experience with various mediums of advertising, and no drug store which follows the suggested lines laid down will go to trouble in vain.

Regarding newspaper advertising, Dr. Diner was both brief and inconclusive. He suggested that the average drug store could not use the newspaper columns in the larger cities to advantage, because of the great loss in circulation values, that would necessarily result.

This criticism, if made to apply to the corner drug store in the residence section, or a store that has but a limited clientele, is, of course, correct. It is foolish to pay for 50,000 circulation, when it is expected only to reach five or ten per cent. of prospects with a selling argument.

But this must not be applied to drug stores or to any other business that operate in the central commercial district or to those institutions which have branches radiating from a central location. For after all is said on the subject of advertising, the newspaper columns must still hold the supremacy for reaching the people. Dr. Diner admits the power of the press when he advises druggists to watch the news columns of local papers to secure notices of births, in order that postcard greetings may be sent to the new parents. For this and similar reasons, the entire public of a city are constantly watching the columns of the press.

Timeliness of advertising is its greatest virtue; and to the store that has daily or frequent "specials," new trade can always be developed by a well-displayed advertisement in the newspapers. Thousands of people in this day and time do all their buying before they leave home, by picking out from the papers just those things that are listed for which they have need.



But the newspaper will not do away with the need for other mediums of advertising, as Dr. Diner has well shown; and it is with the combined aid of the press, of attractive show windows, of well arranged store interiors, of personal advertising, of special mailing lists and of jam-up service, that the progressive druggist must build his larger success.

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## THE ECONOMIC VALUE OF THE WHOLESALE DRUGGIST.

In the May, 1918, number of this JOURNAL, page 397, reference was made to the announcement of a prize contest inaugurated by the National Wholesale Druggists' Association, the prizes consisting of various sums ranging from \$150 to \$20, to be awarded for essays written by traveling salesmen on the subject of "The Economic Value of the Wholesale Druggist and Reasons Why He Is Essential." The committee who acted as the judges in this contest were Mr. Walter V. Smith, of Philadelphia, Mr. J. K. Lilly, of Indianapolis, and Mr. F. H. Garrett, of Council Bluffs. They awarded the first prize, \$150, to O. B. Wells, of Albany, the second prize, \$100, to H. B. Rhoads, of Indianapolis, the third prize, \$50, to H. S. Godshall, of Philadelphia, the fourth prize, \$30, to J. F. Beerke, of Omaha, and the fifth prize, \$20, to Joseph Bailey, of Kansas City, Mo.

These prize-winning essays have been published in pamphlet form and distributed by the N. W. D. A. and well merit careful perusal. The space available permits only of brief abstracts from these.

From the first of these essays the following abstract is given:

"The rôle of the wholesale druggist is of a double nature. His work is for the manufacturer as well as the retailer. He brings to the counters of thousands of retail druggists the products of innumerable manufacturers. Distribution is the keystone of successful business, and the manufacturer finds a quick and inexpensive distributing agent for his product in the wholesale druggist.

"The saving of overhead and selling expense which is effected by the wholesaler for the manufacturer is of considerable importance from the producer's standpoint. It is possible to greatly reduce the selling organization and simplify the credit department. An intricate and expensive accounting system no longer becomes

necessary, for business is done with a single wholesaler whose responsibility is above reproach.

"In the foregoing we have considered the economic value of the wholesaler to thousands of manufacturers. This is an important reason for his existence. Now let us consider his relations to the retail trade.

"One of the great advantages of the wholesale druggist to the retailer is the saving of time. One order placed with the wholesaler brings one composite shipment of assorted goods, that might otherwise of necessity be ordered and shipped from a score or more of houses, some of them at great distance from the retailer. The time saved in ordering and receiving goods makes for a quicker and more satisfactory service, and service is the superstructure of all retail trade.

"Consider, too, the time saved in keeping accounts with a single company instead of a large number of concerns. There is less likelihood of a mistake in adjusting claims, and difficulties of any nature can be settled more readily and with much less effort, if the retailer is dealing with a single company.

"Turnover and quick service are the potent factors in making the retail business a successful enterprise.

"Another point is the advantage to the retailer of the wholesale drug salesman. The 'see you next week' representative of a wholesale concern is of vastly more value to the retailer than is generally realized. In the salesman the retailer has a warm friend. The interest the salesman has in his trade, his good advice, his trade tips on prices, advances, declines, market conditions and what-not make for a splendid cordiality and help to build up an 'over the top' spirit which is bound to win.

"The retailer is not entirely dependent upon his own judgment in placing orders for goods, for the knowledge the salesman has of the goods and demands of the retail trade may be depended upon in those matters. The wholesaler keeps up the quality of goods for the retailer. He makes it his business to make a study of the quality of his goods. Thus the wholesaler and retailer coöperate to give the best possible service to the patrons of the retail trade—the consuming public.

"Every retailer is dependent upon some system of credit in purchasing goods. If there were no wholesale drug concerns the

retailer would very likely be obliged to establish and maintain credit with a large number of manufacturing companies. Such a condition would entail a large amount of clerical work, long delays, misunderstandings and dissatisfaction to all parties concerned. On the other hand, it is a comparatively easy matter to furnish reference and make necessary banking arrangements to do business with one company.

"Another expense which the wholesaler saves the retailer is that of accounting. The bookkeeping necessary when the druggist makes use of the wholesaler can be done easily and without inconvenience by the retailer himself. Thus a great saving is effected.

"So it is obvious that the wholesaler stands to the retailer in the same relation that the retailer stands to the consuming public. He is indeed a necessity, an economic asset, an entity of great importance and great worth."

From the second of these essays the following abstract is given:

"There has been a great deal said and written in the past few years about the elimination of the middle man, or more direct routing of commodities from the producer to the consumer. The term 'middleman' is a misnomer. The proper word is 'distributor,' for that is his function. A great deal of the speaking and writing has been done by demagogues, visionaries and people unfamiliar with trade relations and requirements. Theoretically, it would be a fine thing for the producer to hand his product directly to the consumer and so eliminate the just toll taken by those who would normally assist in its distribution, but in practice it would be, in most instances, an impossibility.

"Considering the volume of business he does, the druggist probably stocks a greater number of items than any other merchant. Every country on which the sun shines contributes to his stock. 'No merchant sells more diversely borne nor more widely traveled merchandise than the pharmacist.' Earth and sea, flora and fauna, raw material and finished product are all found in his stock; and the assembling of the six or seven thousand different items represented in a well-stocked retail drug store, without the aid of the wholesaler, would be a physical impossibility.

"The wholesaler bears the same relation to the retailer that the ordnance and quartermaster's departments bear to an army. When Foch started his offense against the Germans he would never have



succeeded if he had had to replenish his supplies of ammunition, food, etc., from their source; but back of the line were vast stores of these essentials, and as they were needed they were brought up and the guns and the men kept fed. There was never a pause in supplies of materials needed. The men on the firing line knew that what they needed would be at hand when and where it should be. Their time and endeavor could all be concentrated on making use of the material. The retailer is on the firing line and can concentrate on his selling, knowing he can replenish his stock from his wholesaler as he needs the goods.

"No more vital and interesting question confronts the retail druggist than that of turnover. To insure quick turnover the retailer must buy frequently and he can do this only by depending on the wholesaler. Dollars ought to be made to work. A dollar that is not working is a slacker. A retailer that is not working is a slacker. A retailer who turns his stock four or five times a year, if he makes a legitimate profit, will make money. The man who turns his stock twice, or less—and many do no better than this—can not make money.

"The secret of success in selling merchandise is to buy often and get your money back to reinvest.

"The wholesaler, through his connection with sources of supply, comes into possession of information which he in turn passes on to his customers, enabling them to buy and sell to greater advantage. Just since the war began the drug wholesalers of the country have saved their customers thousands of dollars by advising them as to their buying, and impressing upon them the importance of adjusting prices to market values, and enabling them thus to obtain the legitimate profit to which they were entitled. When the retailer is threatened with legislation that menaces his business the wholesaler is always called as 'first-aid.'

"The wholesaler is a clearing house for the things the retailer wants to know. Suppose the retailer were buying direct from dozens of concerns all over the country. No one of them would be sufficiently interested to render this service. And personal service does appeal to the customer. Many druggists could not get along without it.

"In conclusion the wholesaler is essential because he is equipped and organized to render the thing most vital to the retailer—service."

From the third of these essays the following abstract is given:

"The economic value of the wholesale druggist is primarily based on service; therefore, he is essential in direct proportion to the amount of service he renders.

"It is the duty of the wholesalers to serve directly two important classes of business: the producer or manufacturer and the retail distributor, and indirectly the consuming public.

"The large producers of proprietary articles who advertise nationally recognize the fact that thorough distribution is absolutely essential in any advertising campaign to make it successful. The quickest and most economical distribution is undeniably through the wholesaler.

"The facilities of the wholesale druggist mean for the manufacturer: (1) Widely separated distributing points for the manufacturer's goods subject to immediate delivery to cities, towns and hamlets everywhere. (2) The opportunity of connecting up and keeping abreast with an advertising campaign in any section of the country through the frequent visits of the wholesaler's sales force. (3) The responsibility in collecting for the sale of merchandise to the retailer. (4) Concentration and economy in shipping goods to central distributing points. (5) Prompt payment of the manufacturer's bill.

"These are all of them positive and indisputable benefits to the manufacturer.

"For this service, the wholesaler receives a trade discount from the manufacturer's list price and in most instances a discount for prompt payment of the manufacturer's invoice, which is his remuneration for the handling of this class of merchandise, and from which he must pay all his overhead costs of handling the goods and have something left for profit.

"Without the service of the wholesale druggist, the manufacturer would be compelled to do many things: (1) To establish selling agencies in various sections of the country with heavy overhead costs. (2) To employ a large sales force, to cover the entire country, at high salaries, and heavy traveling expenses. (3) To carry many accounts on his books with a high cost of collection. (4) To ship small lots of goods to all sections of the country at a big expense and enormous detail. (5) To have his money tied up in numerous accounts and lose the advantage of ready capital.



"These points make it very clear that the wholesaler derives his profit only out of the saving he affords the manufacturer or producer.

"The wholesaler serves the retailer in many ways: (1) He supplies him with upwards of 2,500 articles in one shipment with little capital outlay, and replaces them at short notice on re-order, giving the retailer the advantage of a frequent turnover; a concentration of freight bills to a minimum cost and he eliminates them altogether if located in the same city. (2) He collects drugs from all parts of the world, guaranteeing quality, freshness and analysis for standard requirements. (3) He extends credit when credit is needed. (4) He facilitates a quick and easy adjustment of claims. (5) He watches the market for new goods and keeps abreast of the times so that the retailer may obtain with dispatch and economy small amounts of newly advertised goods. (6) He maintains a well-posted sales force not only to show and sell goods, but to impart trade information, give advice and keep retailers posted on federal, state and municipal legislation, and to look after his interest in general.

"These are the reasons why the wholesaler is essential to the retailer in the scheme of present-day merchandising, and without him, it seems very clear that chaotic conditions would face the retailer."

From the fourth of these essays the following abstract is given:

"The wholesale druggist is essential, and renders an economic service which is three-fold: he serves the manufacturer, the retailer and the consumer. The wholesaler acts as warehouseman, and is as necessary to the manufacturer as the clearing-house is to the bank.

"By marketing his product through the wholesaler, the manufacturer reduces overhead expenses in all the departments of his business, with the possible exception of the advertising department.

"It is through the wholesaler and his salesmen that the manufacturer gets his product on the shelves of the retail druggist in the city and country, and at a lower distribution cost than he could otherwise obtain. He has no occasion to worry over the collection of accounts, as the wholesaler either discounts his purchases, or pays them at maturity, which is not the case with the average retailer.

"If there had been no wholesalers during war times, a great number of the retailers would have been obliged to close their



doors, as it would have been impossible for them to keep up stocks. As it was, all they had to do was to look pleasant, as their good friend, the wholesaler, did the worrying, and in those days there was cause for it. The average retailer does not appreciate that today the wholesaler has to pay spot cash for much of his merchandise. Nor does he know the amount of money the wholesaler has tied up without a chance of turning a dollar of it over for months at a time. He gives the retailer dating on this same merchandise for which he has to pay spot cash, and all for the sake of rendering an economic service. The retailer certainly could not get this same service by buying direct from the manufacturer or direct-selling house.

"Who kept the retail druggist posted as to all the rapid price changes during the four years and a half of war? advised him what, how and when to buy? kept him informed as to all the new government regulations and rulings that affect his business, in order to keep him out of trouble? Was it the manufacturer—or any of the direct-selling organizations or their representatives? No, it was through the wholesaler and his representatives that he got all of this information.

"And now when business conditions are changing and stock is low and prices declining, the retailer will have to lean more upon the wholesaler than he did before or during the war for the adjustment of his business affairs.

"Statistics show that it costs the retail druggist about 35 per cent. for overhead expense. If there were no wholesalers of drugs, and the retail druggist had to buy everything direct from the manufacturer, it would increase his overhead at least 10 per cent., which would make 35 per cent., on account of extra expense for stock clerks, floor space, increased stock, depreciation, express and freight charges, and many other items of expense, which he does not have to bear in buying from the wholesaler. The ultimate outcome of all this would be that the dealer would have to raise his selling price to the consumer, as the average gross profit for the retail druggist is  $33\frac{1}{3}$  per cent.

"The wholesale drug salesman is the connecting link between the manufacturer, wholesaler, retailer and consumer. The wholesaler relies upon his salesmen to present his special lines to the retailer and to adjust difficult matters pertaining to accounts, short-

ages, breakage, returns, etc., as the average retailer is a poor correspondent. The retailer relies on the drug traveler to bring him news of events affecting his business.

"Many retailers are not good stockkeepers, and were it not for the presenting of seasonable things in rotation by the drug traveler they would, generally speaking, be buying holiday goods the day before Christmas, and everything else in a similar manner. It is here that the customer is accommodated, as it is through the efforts of the drug traveler that he is able to purchase the latest commodity when he wants it."

From the fifth of these essays the following abstract is given:

"The principle of distribution operates in the normal processes of nature. The elements of bone and tissue in the animal economy, and, in a sense, fluid and fiber in the vegetable, are assembled at a common center from numerous sources and thence distributed to every part. When this process is functioning properly we have health and development, but when interrupted, decay ensues.

"So in the commercial life—particularly as it pertains to the drug business—the same processes are essential to a wholesome condition and a perfect balance.

"The wholesaler himself recognizes the advantage of this process and is in his turn, a patron of other distributors still nearer the source of production, such as the importers and brokers in the remote world markets. He does not purchase his cinchona in the forests of South America, nor his opium in the poppy fields of China. Neither does he visit the factories of France to buy their exquisite perfumes or other rare luxuries of the toilet. These are purchased from importers and others who comb the fields of foreign production and assemble them here at points for convenient distribution.

"This he does because no other plan is practical or even possible. And, for the same reasons, the retail druggist must depend upon a like service through his wholesaler.

"Now if the wholesaler were eliminated and the retailer bought direct, this would mean a separate transaction with each of more than a thousand manufacturers, instead of one wholesale house. It would mean many accounts payable on his books where otherwise one would suffice; the writing of thousands of letters in the course of replenishing stock where now an order given the whole-

saler's representative from time to time will accomplish the same purpose. Then again in remitting these accounts it would mean thousands of letters and thousands of drafts instead of a check now and then to the wholesaler. The postage alone in this infinite correspondence would represent no insignificant sum.

"The same multiplicity of detail and labor extends to all lines in the store. Some idea of what this means may be gathered from the statement that the average wholesale drug house carries over forty thousand items in stock.

"Another advantage that must be appreciated by the retail trade is the regular visits of the wholesaler's representative—the salesman. He is only an arm of the wholesaler's service, but as essentially a part of it as is the buying or the shipping departments. The value of his service can not be over-estimated. Every conscientious salesman recognizes that his acquaintance on his particular territory, and the confidence he commands are valuable assets. He also realizes that the better service the more he increases the value of this asset. Consequently it can be relied upon that he will protect their interests in their relation with his house with the same solicitude with which he would treat his employer's interest in the same transaction.

"I have referred to the sameness of interests between the retailer and the wholesaler. In the fever and confusion of business the significance of this is often overlooked. I do not believe the relations between the retailer and wholesaler in any other line of business are so marked by the same splendid sentiments and unselfishness. The wholesaler stands as a ready champion of the retailer's rights. And it can not be alleged that his motives are always mercenary. There is a willingness to respond to his needs; to coöperate with him in every movement that conduces to better business and higher ideals. This is attested by his efforts to discourage price cutting, to keep down unwholesome rivalries, to secure more favorable legislation, to protect against the piracy of mail-order houses, to obtain from manufacturers a scale of prices permitting a more reasonable margin of profit on advertised products."



APPLIED CRYSTALLOGRAPHY.<sup>1</sup>BY HENRY LEFFMANN, M.D.,  
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Crystals are attractive to the learned and unlearned. The crystalline form of any given substance is always more striking than the amorphous form, gives better evidence of purity and serves far better for identification. Most chemists, however, are not deeply learned in crystallographic lore, whether engaged in teaching, research or analyses in the commercial or works laboratory. The pharmaceutical chemist depends to a limited extent on the crystalline form of the common medicinal salts, but it is the mineralogist who has cultivated the science of crystallography to the greatest extent. The crystals of natural minerals are usually so large and so characteristic as to constitute one of the most important means of identification, indeed, this feature has dominated mineralogy to such an extent that it has become largely a science of external form, rather than chemical constitution. The mathematical exposition of crystals is complex and abstruse. Chemists generally take no interest in it. They do not trouble themselves with the mysteries of the basal pinacoid, hemihedral and tetartohedral modifications or enantiomorphism. This is largely due, of course, to the fact that the chemist deals in the main with artificial substances of which the crystals are minute and imperfect, and even when dealing with a crystal of an artificial substance produced on the large scale and, therefore, presenting distinct form, the practical chemist prefers only to rely on chemical tests rather than optical and geometric methods.

The microscope is much more in evidence in the chemical laboratory than it was fifty years ago, but even now in many of its applications no use is made of the valuable accessory appliances that mineralogists and especially petrologists employ. In clinical, physiologic and toxicologic chemistry most workers are still satisfied to describe the crystal forms that they find in the microscope field by such common terms as "stellate," "needle-shaped," "plate-like." We still hear of the "dumbbell" crystals of calcium oxalate—or oxalate of lime, as clinicians persist in calling it—and of the "coffin-

<sup>1</sup> Reprinted from *The Catalyst*.

lid" forms of ammonium magnesium phosphate. The different attitude toward mathematical crystallography on the part of chemists as compared with mineralogists is due to the fact, indirectly mentioned above, that the chemist deals with minute forms, with which our sense of touch is not available. The field of the microscope is practically a two-dimensional space, the full appreciation of a crystal requires its measurement in three directions.

Of late, however, a much more extended application of the microscope to the solution of analytic problems has been inaugurated, and in the course of a few years a vast amount of data of the most valuable type will be obtained. For this special training and highly specialized apparatus is required. Thorough knowledge of the mathematics of crystallography, in the phenomena of polarized light and good technical skill are required. Elaborate equipment of the microscope is needed, polarizing apparatus, selenites and similar accessories, practically unknown to the general analyst and works chemist.

The United States Bureau of Chemistry has been for some time carrying out researches along these lines, and has a special worker, Dr. Edgar T. Wherry, to whom the title of "Crystallographer" has been given. As he was a pupil of mine in his elementary studies in chemistry, and as I have been associated with him in work at the Wagner Free Institute of Science. I have had special interest in his researches. At the meeting of the Philadelphia Mineralogic Society in March last, Dr. Wherry presented some of the results of his investigations. Among these was an ingenious detection of an unusual sugar that had been obtained by the bees of a certain area in the United States through feeding on the honey-dew produced by an immigrant aphid. This sugar was not digestible by the bees and they starved to death in great numbers. Another instance of the use of the methods was in determining the reason for the differences in color in a new high explosive which the United States authorities were making. It was found that the differences were due to inclusions in the crystals.

A remarkable application of x-rays to the study of molecular structure has been discovered and some extremely interesting results are already at hand. So far they have a bearing on theoretical questions only, but chemists know very well how soon pure science may be translated into a practical form. Space does not permit of discussion of these x-ray studies.

The invention of simple processes of color photography has been of great assistance in putting on record the appearance of the microscopic field and enabling it to be shown by means of the ordinary projecting lantern. The effects of polarized light are especially brilliant, and the colors are essential in many cases for differentiation. Many members of the section will recall the series of photomicrographs in color that I showed at the summer meeting at Swarthmore some years ago, although the vividness of the demonstration was seriously impaired by the inferiority of the projecting lantern.

A field that seems to promise much, but has not yet been worked to any extent by the chemist, is the use of ultra-violet and infra-red light for differentiation substances. In the case of the former, photomicrography must be used, as the ultra-violet rays are invisible to the human eyes, and very injurious to it.

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### ANTISCORBUTICS:<sup>1</sup> I.

Ever since Holst and Fröhlich<sup>2</sup> asserted, in 1912, that the antiscorbutic property of certain fresh vegetables and fruits may be to a large extent lost when they are subjected to a high temperature or are dried, students of nutrition have been more alert to the possible effects of culinary processes on some of the less understood properties of foods. Although, as has already been discussed in these columns, McCollum and his colleagues have assumed that scurvy is a disease related to intestinal putrefaction and the retention of feces, the concordant opinion of other recent investigators, notably Givens, Hart, Hess, Mendel, Steenbock and their co-workers in this country, and Chick, Harden and their collaborators in England, has substantiated the earlier view that the disease is the result of a deficiency of some nutritive factor in the diet. From this standpoint we may speak of the lack of an antiscorbutic vitamin, just as the lack of an antineuritic vitamin is postulated in the genesis of polyneuritis.<sup>3</sup>

<sup>1</sup> From the *Jour. Amer. Med. Asso.*, July 26, 1919.

<sup>2</sup> Holst and Fröhlich: *Ztschr. f. Hyg.*, 72: 1, 1912; 75: 334, 1913.

<sup>3</sup> Hess, A. F., and Unger, L. J.: Scurvy, VIII: Factors Affecting the Antiscorbutic Value of Food, *Am. J. Dis. Child.*, 17: 221 (April), 1919. Hart,



The lack of knowledge of the distribution of antiscorbutic vitamins has been accentuated by the needs of infant feeding. The use of cow's milk pasteurized at a temperature as low as 63° C. (145.4° F.) for thirty minutes has led in the course of several months to milk outbreaks of infantile scurvy,<sup>4</sup> thus indicating the poverty of heated milks in the antiscorbutic vitamin. Only recently Hart, Steenbock and Smith have demonstrated at the University of Wisconsin that milk sterilized at 120° C. for ten minutes, commercial unsweetened condensed milk, and the commercial milk powder examined had lost their antiscorbutic properties when used in quantities equivalent to an amount of raw milk which would prevent scurvy in guinea pigs on a diet of rolled oats and dried hay. From such citations it becomes evident why investigators of infant feeding have sought sources of antiscorbutics and why producers of food preparations are concerned with the retention of native antiscorbutic potency so far as this is possible. Recent writers<sup>2</sup> have sanely summarized the situation by saying that either the results with guinea pigs on experimental scurvy should not be translated to infantile scurvy, or we should follow the wiser course of using some antiscorbutic in conjunction with the exclusive use in infant feed of such heated milk products as have been described.

Thanks to the labor of a number of investigators both here and abroad, the pediatrician is no longer limited to the conventional orange juice in his efforts to avert scurvy in infants. Reference has been made in THE JOURNAL to some of the novelties, such as the raw juice of the swede and the tomato, which are also available for human nutrition. Although the antiscorbutic value of fruit juices was recognized three hundred years ago, Alice Henderson Smith,<sup>5</sup> of the Lister Institute in London, has upset the traditional faith in lime juice, as the result of her historical studies. It appears that the juice used with good effect in the olden days was in reality ob-

E. B., Steenbock, H., and Smith, D. W.: Studies of Experimental Scurvy: Effect of Heat on the Antiscorbutic Properties of Some Milk Products, *J. Biol. Chem.*, 38: 305 (June), 1919.

<sup>4</sup> Hess, A. F., and Fish, Mildred: Infantile Scurvy: The Blood, the Blood Vessels and the Diet, *Am. J. Dis. Child.*, 8: 385 (Dec.), 1914. Hess, A. F.: Infantile Scurvy, III, Its Influence on Growth (Length and Weight), *ibid.*, 12: 152 (Aug.), 1916.

<sup>5</sup> Smith, A. H.: A Historical Inquiry into the Efficacy of Lime Juice for the Prevention and Cure of Scurvy, *J. Royal Army Med. Corps*, Feb. and Mar., 1919; *Lancet*, 2: 725 (Nov. 30), 1918.

tained from lemons and sweet limes, not from the West Indian sour limes. With the change to the sour limes has come a failure in antiscorbutic potency that was difficult to understand until it was demonstrated recently by experimental tests on animals that the sour lime of the West Indies (*Citrus medica-acida*) happens to have only one quarter of the antiscorbutic value of the lemon (*Citrus medica-limonum*). Lemon juice is easily available for the treatment of infantile scorbutus. Harden and Zilva<sup>6</sup> have further demonstrated that after removal of the free citric acid and other acids from lemon juice, the residue also retains its antiscorbutic activity; and in collaboration with Still<sup>7</sup> these investigators have, for the first time, clinically employed with success this antiscorbutic factor separated from the greater part of the inactive components in combination with which it occurs. The vitamin-containing product could be administered in large dosage after the refinement and the exclusion of extraneous substances. In fact, the lemon product was given in concentration at least double—in one case seven times—as strong as the form in which it occurs naturally in the foodstuff (lemon) from which it was obtained. The treatment was thus, so to speak, “intensive,” reminding one of the seemingly potent therapeutic procedure of Hess, who introduced orange juice directly into the circulation of scorbutic infants.

There are indications that the potent fruit juices can be suitably preserved for clinical use. This is a matter of no little consequence in conserving products that do not come into the market with uniform frequency and at reasonable prices throughout the year. Harden and Robinson<sup>8</sup> have reported from London that the antiscorbutic principle in orange juice is not volatilized when the juice is distilled at 40° C. under reduced pressure. By evaporation of orange juice at 40° C. under reduced pressure, it is possible to obtain a solid residue which possesses in a very high degree the antiscorbutic value of the fresh juice. This value is not appreciably diminished when the substance is kept in a dry atmosphere at room temperature during six months. The prolonged heating to which

<sup>6</sup> Harden, A., and Zilva, S. S.: The Antiscorbutic Factor in Lemon Juice, *Biochem. J.*, 12: 259 (Oct.), 1918.

<sup>7</sup> Harden, A., Zilva, S. S., and Still, G. F.: Infantile Scurvy: The Antiscorbutic Factor of Lemon Juice in Treatment, *Lancet*, 1: 17 (Jan. 4), 1919.

<sup>8</sup> Harden, A., and Robinson, R.: The Antiscorbutic Properties of Concentrated Fruit Juices, *J. Royal Army Med. Corps*, Jan., 1919.

fruit juices are subjected in the usual processes for the manufacture of jams and jellies renders it unlikely that these would ever possess any considerable antiscorbutic value. Nevertheless, Harden and Robinson have found that by the use of the newer extremely rapid commercial processes of concentration without the application of high temperatures, fruit jellies can be prepared (from the apple, for example) which are by no means devoid of antiscorbutic potency, though this is of a different order from that characteristic of the orange and lemon. Surely there can no longer be any excuse for the failure to avert infantile scurvy, even when fresh, unheated milk is not available.

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## PRODUCTION OF GLYCERIN FROM MOLASSES.<sup>1</sup>

BY ARTHUR R. LING.

In view of the apparent close structural relationship between the monohexoses, glucose, fructose, etc., and glycerin, the conclusion seems justified that it ought to be possible to obtain the latter compound by the fermentation of these sugars under certain conditions with one of the saccharomycetes or yeasts. Nor is this mere speculation, for be it remembered that Pasteur in 1858 observed that glycerin and succinic acid, albeit in traces only, are invariable products of the so-called alcoholic fermentation of the sugars, and this is now a well-established fact. Moreover, there is every reason to believe that the glycerin at all events formed in this way owes its origin directly to the sugars and not to the secondary constituents always present in those fermentable liquids, worts, musts, etc., met with in commerce. In this connection it may be pointed out that F. Ehrlich showed in 1907 that the higher alcohols and esters present in fermented worts and musts are derived from the amino acids and not from the sugars. In 1909 he brought forward evidence that succinic acid is formed in the same manner.

Despite numerous attempts to obtain glycerin in such quantity by the fermentation of sugars that its production in this way would become commercially profitable, no success has up to quite recently been met with.

<sup>1</sup> Reprinted from the *Journal of the Society of Chemical Industry*, May 21, 1919.



A report from the Laboratory of the Internal Revenue Bureau, Washington, dated May 6, 1918, has within the past few days been placed in the hands of the writer. In it experiments are described indicating that the problem of the production of glycerin by the fermentation of sugars in such a yield as to be of commercial significance has been solved.

It seems that Dr. Alonzo Taylor, then Assistant Secretary of Agriculture, reported that when in Germany in the summer of 1917 the Germans were producing glycerin in large quantities by a fermentation process. Investigations were undertaken at four different laboratories in the United States with a view to elucidating the problem, and Mr. A. B. Adams, Chief Chemist of the Laboratory of the Internal Revenue Bureau, Washington, was able to report to the Hon. Daniel C. Roper, Commissioner of Internal Revenue, three months after the work had been assigned to the laboratory, that Mr. John R. Eoff had solved the problem in so far that he was able to produce glycerin in such quantities that if the actual cost of the recovery was not too high the process would be commercially profitable. Details of the process have been furnished to the British and French authorities, and to interested manufacturers in the United States.

The report in which the experiments are described in detail is signed by Messrs. John R. Eoff, W. V. Linder and G. F. Beyer.

After numerous trials with pure cultures of different yeasts, *Saccharomyces ellipsoideus* (var. *Steinberg*), No. 657 of the collection of the American Museum of Natural History, New York, was selected as most suitable. Preliminary experiments were then instituted which ultimately led up to the following general conclusions:

The best yields of glycerin were obtained by fermenting solutions of sugar containing 5 per cent. of sodium carbonate, which must not be added to the liquid all at once. A less quantity of the alkali diminishes the yield of glycerin, while a larger quantity stops fermentation. Other alkaline substances, sodium hydroxide, potassium hydroxide, and borax may be used, but sodium carbonate (soda ash) is preferable on account of its cheapness. Although no hard and fast rule can be laid down for the method of adding the sodium carbonate, which must be varied according to the nature of the sugar solution, it should be added as soon as the fermentation has well started, and in as large quantities and as frequently as is

possible without stopping fermentation. The earlier the addition of the alkali, the higher the yield of glycerin will be. It is necessary that the yeast be "worked up" by making a "bub," and it has been observed that the presence of ammonium chloride in the fermenting liquid augments the yield of glycerin. The most favorable temperature for the fermentation is 30–32° C., and the fermenting liquid should not vary from these limits of temperature for any considerable period. Higher temperatures lead to a loss of alcohol and glycerin, and to the formation of objectionable substances, whilst smaller yields of glycerin are obtained at lower temperatures. The most favorable concentration for the sugar solutions lie between 17.5 and 20 Gms. of sugar per 100 Cc. It has been found that when fermentation is complete according to the method above outlined, 20–25 per cent. of the sugar originally present in the liquid is converted into glycerin, and practically all the remainder into alcohol and carbon dioxide. The nature of other substances which are formed has not yet been determined. It is mentioned that when the sodium carbonate has been added to the fermenting solution in sufficient quantity, a copious precipitate is formed, the evolution of gas ceases, and the yeast apparently lies dormant for a while. The precipitate eventually disappears and the fermentation again proceeds. It is essential that this precipitate should form, and that the fermenting liquid lie quiescent for a while. The addition of the sodium carbonate in solid form has been found to produce better results than if it be added in the form of a solution.

A description is next given of the process as carried out on a commercial scale, using inedible "black strap" Porto Rico molasses.

The yeast starter or "bub" is first prepared in the following manner. Yeast No. 657 (see above) was seeded with a platinum loop into 150 Cc. of sterile grape juice, and allowed to ferment to the final degree. Fifteen Cc. of this was then added to 150 Cc. of sterile grape juice, and when fermentation had finished 75 Cc. was added to 800 Cc. of a solution of sterilized "black strap" molasses at 21.2° Balling (about sp. gr. 1.085). As soon as brisk fermentation had set in, 3 Gms. of soda ash was added and the bottle shaken until solution was complete. After fermentation had resumed, and when it had reached its final point, the whole of the liquid was added to 2 gallons<sup>2</sup> of a similar "black strap" molasses solution,

<sup>1</sup> The gallon referred to in this article is the U. S. gallon. The factor for the conversion into the British gallon is 0.834.



and this was treated at the proper time with soda ash in the same proportion as before. Fermentation being complete, the whole two gallons was added to 40 gallons of a solution made as follows:

"Black strap" molasses was dissolved in sufficient water to make 425 gallons of wash at 21.2° Balling at 25° C. Eight pounds of ammonium chloride was added, and after the liquid had been sterilized sufficient sterile water was added to bring it back to the original density. This solution contained 16.85 per cent. of sugar. The following are the details of the main fermentation:

17.II.17., 9 A.M.—40 gallons of wash (see above) seeded (see above).

3 P.M.—2 lb. soda ash added.

9.15 P.M.—The 40 gallons added to 385 gallons molasses wash.

18.II.17., 12.30 A.M.—Added 24 lb. soda ash (T. 30° C.).

3.30 A.M.—Added 36 lb. soda ash (T. 31.5° C.).

5.30 A.M.—Added 48 lb. soda ash (T. 33° C. Attempted to 30° C.).

11 A.M.—Added 48 lb. soda ash (T. 32.5° C. Attempted to 30° C.).

5.30 P.M.—Added 36 lb. soda ash (T. 32° C. Attempted to 30° C.).

The fermentation was then allowed to proceed to completion, which took five days, the temperature being kept at about 30° C.

At the conclusion of fermentation the wash was analyzed and the following results were obtained: Glycerin, 3.1 per cent. by vol.; alcohol, 6.75 per cent. by vol.; sugar (apparent), 0.86 per cent. by vol.; alkalinity, 3.6 Gms.  $\text{Na}_2\text{CO}_3$  per 100 Cc.

The purification of the fermented wash was then carried out as follows: 3,200 lb. of the wash was neutralized in a tank with sulphuric acid, and 12 gallons of a saturated solution of commercial ferrous sulphate (copperas) added. The wash having been brought to near the boiling point, milk of lime was added until there was an excess of lime in solution, when the wash was boiled for half an hour by means of a steam coil. The liquid was next passed through a filter press, and the cake steamed. The copperas and lime treatment was then repeated, and after again being passed through a filter press the alkalinity was brought to 0.2 per cent. ( $\text{Na}_2\text{CO}_3$ ) by the addition of soda ash. It was then filter pressed



and steamed, and the filtrate evaporated in a vacuum evaporator to a thick syrup which contained between 30 and 35 per cent. of glycerin. It was then distilled in a still resembling that of Jobbin. About 50 lb. of dynamite glycerin was thus obtained, or roughly about *half that present in the fermented wash*.

The following is an analysis of a sample of the dynamite glycerin:

Sp. gr. at 15.6° C., 1.2616; carbonaceous residue, 0.058 per cent.; ash, 0.009 per cent.

The carbonaceous residue is high, but a redistillation of the glycerin gave a satisfactory product. The glycerin was found to nitrate normally.

It is noteworthy that it has been found that the second treatment of the fermented wash with copperas and lime is superfluous. Hitherto it has not been found possible to obtain a perfect crude glycerin from molasses.

Several additional experiments have, it is stated, been carried out on a much larger scale—2,000 gallons—with the same results.

It will be remembered that in an earlier part of this report it was mentioned that from 20–25 per cent. of the sugar originally present in the mash is converted into glycerin. Taking the sugars actually fermented in “black strap” Porto Rico molasses as 50 per cent. of the molasses (and this is a very liberal estimate, for it may be computed from the figures given that nearly 3 per cent. of the sugar in the molasses is left unfermented), and remembering that only half the glycerin formed is recovered as crude glycerin, the yield of glycerin could not be expected to exceed 5½ to 6 lb. per cwt. of the molasses dealt with. It is only fair, however, to quote the following remarks of the signatories of the report. They say:

“It must be borne in mind that there is considerable alcohol produced in these fermentations. At the present price of alcohol and raw materials it is safe to say that the value of the alcohol balances the cost of all material and overhead charges entering into the production of the fermented mash. This being true, then the slop from the alcohol distillation which contains the glycerin is had free of cost, so that the only cost to be considered for the glycerin would be that of purification and distillation. This should not be great. No attempt has been made as yet to recover the alcohol, it being deemed a matter offering no difficulty.”

Experiments have also been carried out on a large scale using cane sugar and starch glucose as fermentable material. It was found, however, necessary in these cases to employ yeast foods in quantities that deleteriously influenced the purification of the glycerin. It was therefore concluded that these materials possess no superiority over molasses for the purpose.

Since the process of producing glycerin by fermentation is in its present state of development restricted to molasses, the writer would point out that in some parts of the world, notably in Australia and Fiji, molasses is a waste product which is run out to sea. The present process should, therefore, be of great significance in such countries. There are several details in this process, as outlined in the report, which in the writer's opinion are open to criticism. As, however, a year has elapsed since the report was officially handed in, further developments may have eliminated the applicability of these criticisms.

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## COLLOIDAL METALS: THEIR PREPARATION AND PROPERTIES.<sup>1</sup>

BY THOS. STEPHENSON, F.R.S. EDIN.

The use of colloidal substances in medicine is of comparatively recent introduction, and now that knowledge of their properties and action is more exact, their employment in the treatment of disease is increasing rapidly. It is intended here to give merely a general sketch of the colloidal preparations in more general use: for details of the various varieties of colloids readers are referred to the very complete section on this subject in the Extra Pharmacopœia by Martindale and Westcott (16th edit., p. 308).

The term "colloid" (from *κολλα*, glue) was first used by Thomas Graham to distinguish those amorphous substances, of which glue and gelatin are typical examples, which diffuse with difficulty through membranes, as opposed to "crystalloids," which diffuse with ease. The word is now used to describe a condition which chemical substances may be made to assume, rather than to define a particular class of compounds. A colloidal solution is in reality a suspension of minute particles of the substance. These particles are

<sup>1</sup> Reprinted from *The Prescriber*, June, 1919.

charged with positive or negative electricity, and the passage of an electric current through the solution causes the particles to move respectively towards the cathode and the anode. Some colloidal solutions are readily precipitated by heat or by mechanical means, and, as will be seen later, this has to be guarded against in their therapeutic application.

The nature and properties of colloids and of colloidal solutions have been known for some time, but the assumption by the metals and metalloids of the colloidal state is a comparatively recent discovery. It is these that have come into extensive use in medicine. The first metal to be used in this way was colloidal silver, which, in 1896, was introduced into therapeutics under the name of "collargol." This substance, which occurs in small black scales having a metallic lustre, forms with water an opaque solution, which has all the properties of a colloid. Collargol, however, is not really a colloidal metal, but is generally considered to be a combination of an acid silver molecule with ammonia, *i. e.*, collargolate of ammonia.

Shortly after the introduction of collargol, Trillet succeeded in preparing oxydases of certain metals by precipitating solutions of metallic salts with an alkali in presence of albumin, forming a kind of colloidal solution of the metals. Later, Bredig produced the solutions known by his name. These are true colloidal "solutions" (or suspensions) of the metals, and are produced by passing an electric current through pure water between electrodes of the metal to be dissolved. The current diffuses a minute quantity of the metal throughout the liquid—the metal, in fact, becomes volatilized in the liquid. The resulting solution is in every case a dichroic liquid, transparent to transmitted light, and opaque to reflected light. Suspended particles can be detected only by the ultra-microscope, and the solution in all respects obeys the rules laid down for colloidal substances. The metal is in a state of very minute subdivision, and the particles possess that vibratory motion known as "Brownian movement." Different metals have been used in the preparation of such solutions, and more recently colloidal solutions of the metalloids, such as sulphur and iodine, have also been prepared.

In addition to the electrical method for the preparation of colloids, there is the chemical method which has come into fairly general use also. This usually consists in the reduction of a metallic salt by a suitable agent in the presence of a protective colloid such



as gelatin or gum, and the subsequent removal by dialysis of the by-products.

The great difficulty which attended the use of electrically-prepared colloids on their introduction was their instability. The particles had a natural tendency to agglutination, and, in consequence, the solution did not remain therapeutically active for more than a few hours. The usual methods of preservation appeared to be useless. Sterilization by heat caused the particles to agglutinate, and the same result followed the addition of a foreign substance, such as sodium chloride. When injected into the blood, the colloidal solution at once agglutinated, and any therapeutic action was consequently nullified. It was found, however, that the introduction of a small proportion of another colloid, such as gelatin or gum, prevented this agglutination, and the addition of such substance, known as a "protective colloid," has allowed of these preparations being preserved and isotonized for therapeutic use.

For a time it was thought that the therapeutic action of these colloidal solutions was merely catalytic or mechanical, but it is believed now that other factors are responsible. The results recorded of colloidal sulphur in the treatment of rheumatism; of colloidal silver in gonorrhœa; of colloidal antimony in kalaazar, all point to an intensification of the specific action of the metal, which is probably in the ionic condition. Be that as it may, the fact remains that whereas it was originally thought, and probably with some reason in the case of Bredig's solutions, that the actual metal employed was immaterial, it is now known that the different colloidal metals have different therapeutic effects, and cannot be employed indiscriminately.

Of the chemically produced colloids the principal are arsenic, antimony, copper ("cuprase"), gold, iodine, iron, mercury, platinum, selenium, silver, sulphur. "Oscols" and "collosols" are chemically prepared colloids, the names being the property of certain manufacturers.

Electrically produced colloids include copper, gold, mercury, selenium, silver, etc. The products on the market are styled "electr-,"—thus electragol (silver); electraulol (gold).

Under the name of "organosols," Martindale describes colloidal metals obtained by impregnation of lanolin with an aqueous solution of the salt of a heavy metal, and subsequent trituration with a

solution of alkali hydroxide. Double decomposition occurs, and the oxides or hydroxides of the heavy metals are obtained as colloids. The product may be dissolved in ether, in fats, or in liquid paraffin, the cholesterol acting as the protective agent.

Improvements in the preparation of colloidal metals for use in medicine are constantly being announced, and there is little doubt that these substances are destined to play an important part in therapeutics in the near future.

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### GERMAN POISON-GAS FACTORIES.<sup>1</sup>

The Allies in occupation of German territories have the right of access to the German chemical factories situated in the area, and an Inter-Allied Commission has visited the principal works devoted to the manufacture of dyes, medicinal products and standard chemicals. During the war these were occupied with the production of poison gas used in warfare. Major Theodore W. Sill, reporting on his visit as a representative of the United States on the Inter-Allied Commission, reports that, notwithstanding the air-raids to which the factories were subjected, these German plants, "probably the greatest of the potential possibilities for war-material production," are "in splendid condition with a large, highly trained force of employees, and, moreover, with additional opportunities for increasing their production by utilizing the extra equipment added for war-material production." The lack of oil and greases for lubrication of the machinery is the only apparent handicap in the factories. Major Sill warns the American people that this German industry is "a dangerous factor in the struggle for commercial supremacy, and also a potential source of war-material production unless properly controlled." The report (*Journal of Industrial and Engineering Chemistry*) then describes the visits paid to the various poison-gas factories.

"Arriving in Cologne, we made our headquarters there while making a tour of investigation through the plant of the Farben-fabriken vorm. Friedrich Bayer & Co. at Leverkusen, and also the plant of Weiler-ter-Meer at Uerdingen-on-the-Rhine.

"The plant of the Bayer Co. stands out preëminently as the best

<sup>1</sup> Reprinted from *The Chemist and Druggist*, June 28, 1919.

and most modern of German chemical plants. It is a veritable city in itself, well laid out, with excellently constructed streets and brick buildings. Their office building and recreation buildings for the employees are luxurious palaces. This plant has expanded considerably during the war, and, despite the contrary assertions of its directors, was widely engaged in the manufacture of war products, particularly poison gases. We had the opportunity of meeting Dr. Duisberg, the chief director, and incidentally, one of the ex-Kaiser's right-hand men in the development of the war. Many will remember him from his visit to this country at the time of the Chemical Congress in 1912. Incidentally, he hopes to be over here again very soon to see his 'old-time friends.'

"The plant of Weiler-ter-Meer at Uerdingen is also an excellent development, kept up in very good condition. . . . Of all the men whom we met in the various plants in Germany, the head of this plant was the most cordial and open in all his dealings with us. It was, of course, a difficult and humiliating position for men to be in, and in many cases we encountered sullen indifference, particularly among the plant directors, but among the lower classes of foremen and workmen there does not seem to be a general recognition of the fact that the war has been lost and also that the cause was wrong to start with. . . . After spending a few days in Coblenz . . . we journeyed up the Rhine to Mayence, the headquarters of the French area. Within this area we were privileged to visit the Kalle plant at Biebrich. Very little war work had been done at this place, and the plant was probably the poorest of all we saw, being old, dirty, and in a run-down condition.

"At Hoechst-on-the-Main we went through the great plant of Meister, Lucius and Brüning, who were the pioneers in the development of German poison gases, and had done considerable work in all kinds of war material. They, too, had a large, very fine plant, well laid out, and in good operating condition, extending for many acres along the river. They are quite progressive and have developed on a large scale.

"A little later we went up to the greatest of all plants, the Badische Anilin und Soda Fabrik at Ludwigshafen. This plant employs about 16,000 men and covers many acres of ground. They have the plant for dyestuffs, intermediates, etc., at Ludwigshafen, and a little further up the river, at Oppau, is located the plant for the Haber process. Considerable work on war products was done at Ludwigs-



hafen, but they also were able to make dyestuffs on an appreciable scale during the war. At the present time they have a large stock on hand ready to turn loose on the markets when permission is granted. They, too, had done considerable work on poison gases and explosive intermediates, but not to an extent which would at all interfere with their resumption of dyestuff manufacture on a large scale.

"At Oppau we saw what is probably the most phenomenal scientific development up to date—namely, the practical realization on an operating basis of the Haber process for ammonia production. The buildings are all quite new and well constructed, and the vast amount of detail has been studiously and carefully worked out on a practical operating basis, producing upward of 100,000 tons of ammonia per year. This plant was a large factor in enabling Germany to stay in the war as long as she did, by means of producing large quantities of nitrates. The Germans have also another plant, a duplicate of this, which they are operating in the unoccupied area of Germany, so that it is really a great practical possibility at the present time. Incidentally, it came to our attention that Haber, to whom Germany owes so much of her development in chemical products in warfare, had never attained a higher rank than captain in the German chemical warfare service, despite the responsibility and immensity of his job.

"Looking at our inspection of the German plants from a general viewpoint, it is my opinion that, considering the advantage gained in America by the last four years of experience in chemical manufacturing and the lessons learned by our equipment manufacturers, the German plants at the present time from an equipment standpoint and general layout are not superior to the existing American development, their advantage being that they have an experienced and long-trained personnel schooled and willing to carry on the laborious details; but if our people here at home will encourage our new, rapidly growing industries, there is no reason why our own personnel cannot equal or, in fact, surpass that of the Germans.

"There are but few distinctive features to be observed which might advantageously be adopted in some American plants. For instance—(1) the Germans have a very clever method of building their water-towers around the power-house chimneys or stacks, thus utilizing the waste heat and keeping their water from freezing; (2) they have a method of distributing the pressure in the filter presses

so that it is not only applied at the center by a large screw, as in most of our presses, but also horizontally along the sides of the press; (3) at one place we saw an excellent automatic nitration system, based upon the alternate filling and refilling of a small tank with a measured quantity of water, which in turn was connected with valves releasing definite amounts of acid and benzol; (4) the Germans have in practically all of their plants a very high grade of lead fittings, in which art they have advanced remarkably well; (5) in many cases it was also noted they used square flanges on the elbows for their high-pressure piping connections. On the other hand, one notices considerable lack of conveying equipment, such as bucket elevators and belt conveyors through these plants, the probability being that they utilize man power much more than we do, and do not rely upon mechanical equipment so much. . . .

"Among the developments to be noted during the war in Germany, which are of special interest, was the production of synthetic rubber on a large scale and a practical basis. This was done at the Bayer plant in Leverkusen, and the production, though very expensive, was of material assistance in meeting their great shortage of rubber."

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## URANIUM AS AN INDUSTRIAL POISON.<sup>1</sup>

Certain toxicologic effects of salts of uranium have long been recognized and applied in the study of experimental physiology and pathology. Recently industrial conditions have arisen which may place this element in the class of possible dangers of occupation. Karsner and his collaborators<sup>2</sup> of the Western Reserve University School of Medicine, Cleveland, have asserted that in certain industries uranium is employed or appears as a by-product, and that with war time scarcity of some other heavy metals, such as tungsten, uranium may be utilized as a partial substitute. In the production of radium, uranium oxide is produced in large quantities, and if

<sup>1</sup> Reprinted from the *Journal of the American Medical Association*, June 28, 1919.

<sup>2</sup> Karsner, H. T., and Reimann, S. P., "Studies of Uranium Poisoning. I. The Toxicity of Certain Water-Insoluble Salts of Uranium," *Jour. Med. Res.*, 39, 157 (Nov.), 1918. Karsner, H. T., Reimann, S. P., and Brooks, S. C., "Studies of Uranium Poisoning. II. The Solubility of Uranium Oxide in Artificial and Human Gastric Juice," *ibid.*, 39, 163, 169, 177 (Nov.), 1918.

uranium were employed in the steel industry the high temperatures used would lead to the formation of one or several oxides, the most important being uranium dioxide and uranous uranate, both of which are insoluble in water. In grinding, polishing, and perhaps in other operations, these oxides might appear in the form of a dust.

Animal experiments conducted by the Cleveland pathologists demonstrate that uranium oxide, the state in which the metal is most likely to reach the upper respiratory tract when distributed industrially in the form of dust, can be toxic and fatal when administered by mouth. This oxide is insoluble in water; but it will dissolve in gastric juice, so that the possibility of the formation of a soluble toxic salt is established. The production of nephritis by uranium salts has long been recognized as an experimental fact, and the method has served to facilitate the study of the pathology of renal functions. Karsner and his associates have observed that the excretion of uranium, so far as it is accomplished, is primarily by way of the kidneys. When functional and anatomic lesions arise in the kidneys through the presence of the poison, the decreased effectiveness of excretion makes matters worse by favoring an accumulation of the metal in the kidney. There is, probably, no special "affinity" of uranium for the kidney cells nor any unusual susceptibility to the poison on their part. The possibility of protecting the kidneys by the administration of alkalies to combat the concomitant acidosis in such cases represents one of the therapeutic considerations that experimental medicine has taught.<sup>3</sup>

Incidentally it should be stated that uranium nitrate was admitted to the Ninth (the most recent) Revision of the U. S. Pharmacopœia. Surely the danger of this salt could not have been appreciated when this action was taken by the Revision Committee. There does not appear to be sufficient evidence of its therapeutic value to warrant inclusion in this official book. The drug is not included in the Useful Drugs, prepared by the Council on Pharmacy and Chemistry. The Epitome of the U. S. Pharmacopœia, prepared for the use of physicians by a special committee of the Council on Pharmacy and Chemistry, has this to say under "Actions and Uses": "(Uranium nitrate) . . . has been used, without adequate justification, in the treatment of diabetes and cancer. Solutions are

<sup>3</sup> MacNider, W. deB, "The Inhibition of the Toxicity of Uranium Nitrate by Sodium Carbonate," *Jour. Exper. Med.*, 23, 171 (Feb.), 1916; "Relative Toxicity of Uranium Nitrate," *Jour. Exper. Med.*, 26, 1, 19 (July), 1917.



poisonous and produce glucosuria when injected subcutaneously, even in small doses." Our previous knowledge of this drug, now adequately supported by the work of Karsner, should lead the next Revision Committee to omit the drug from the Pharmacopœia.

## DETOXICATED VACCINES.<sup>1</sup>

The living tissues of man and animals possess the inherent power of manufacturing specific antistances against germs when attacked by them. This peculiar power is so highly specialized that the antistance produced acts only against the infecting germ, and not against any other species. An "antigen" is a substance which, when injected into the living tissues, stimulates the production of an "antibody" towards itself. Each species of germ, alive or dead, is, therefore, a "specific antigen," for when the dead organisms—*i.e.*, a vaccine—are injected, the tissues immediately react and commence to manufacture at once the antistances which destroy the germ, or which neutralize the toxins it develops, and upon this action vaccine therapy is based. However, the germs are so toxic, either by reason of the exotoxins which they excrete, or of the endotoxins which remain enclosed within the stroma of the germ itself, that only small amounts of their dead bodies—*i.e.*, vaccine—could be injected, and so the amount of antistances produced was limited by the toxicity of the germ, thus limiting appreciably the effectiveness of vaccine therapy. To Captain David Thomson, R.A.M.C., belongs the honor of having made a discovery which may have far-reaching effects on the future of curative as well as preventive medicine, by increasing the effectiveness of vaccine therapy. In the course of his investigations<sup>2</sup> he found that the gonococcus was extremely soluble in a weak alkaline solution ( $N/10$  or  $N/20$  sodium hydroxide), but was entirely insoluble in weak acids. Further research showed that the meningococci, *B. typhosus*, *B. Friedlander* and *B. influenza* (Pfeiffer), were all very soluble in weak alkalies. On the other hand, Gram-positive organisms, such as staphylococci, streptococci, pneumococci, etc., resisted the action of  $N$ -sodium hydroxide solution. Further investigations led to the

<sup>1</sup> Reprinted from the *Chemist and Druggist*, July 5, 1919.

<sup>2</sup> *Lancet*, June 28, 1919.

discovery that when a  $N/10$  alkaline solution of gonococci was precipitated by  $N$ -hydrochloric acid, the neutralized supernatant liquid was strongly toxic, and caused a severe reaction when injected subcutaneously; it was, indeed, more toxic than the actual precipitate of the gonococcus substance itself. All germs consist of stroma—*i.e.*, the framework of the organism—and toxin, produced by it. Both are soluble in alkali, but the stroma is precipitated on the addition of an acid, leaving the toxin in solution. The gonococcus, streptococcus, pneumococcus and *B. influenza* are very readily precipitated from their alkaline solution by acid. Captain Thomson has found that the toxin could be removed by simply washing the precipitate repeatedly with a weak acid, such as 0.5 per cent. acid sodium phosphate containing 0.5 per cent. carbolic acid. He prefers to inject the precipitate suspended in the above-mentioned solution to redissolving it in alkali and injecting this alkaline, or neutralized, solution. The use of detoxicated vaccines permits the injection of considerably larger doses than have hitherto been permissible. Apart from its great therapeutic significance, Captain Thomson's discovery of a method of detoxicating vaccines brings us a considerable step forward in elucidating the chemistry of bacilli and of their toxins, as the latter can now be isolated and studied.

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#### PREPARATION OF ALGIN.

Chemists throughout the country will be interested to know that the Hercules Powder Company is devoting a good deal of attention to the extraction of algin from kelp. Algin is a substance whose properties are widely known, being a vegetable gum of extremely high viscosity. Its manufacture and use is on a firm footing in Europe, but so far the industry has never become well established in this country, largely, it is thought, because of difficulties in the way of securing a uniform supply of fresh kelp at a reasonable cost. The experience gained by the Hercules Powder Company in harvesting kelp for the manufacture of war materials has overcome these difficulties as far as this organization is concerned.

There is a wide field of possible usefulness for algin. Algin compounds in general give an exceedingly viscous solution, and for that reason their application as a sizing for textiles and paper, as a thickener for printing colors, and as a proofing for interior walls

and ceilings is at once apparent. The sodium compound of algin is soluble in water, a five per cent. solution thereof being so viscous that it can hardly be poured from a vessel. The compounds of the heavy metals with algin are insoluble in water, some of them being soluble in ammonia, which solvent is used in their application as a waterproofing material in textiles.

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## BOOK REVIEWS.

OPPORTUNITIES IN CHEMISTRY. By Ellwood Hendrick. 102 pages. 75 cents. Harper and Brothers, New York.

This is said to be "a book answering the first question of a man who thinks he wants to be a chemist. It tells him in simple straightforward language what possibilities chemistry offers and how to make a success of it."

The Introduction tells us that all of the good chemists known by the author have been full of curiosity, that the chemist must be imaginative, and, in order to have joy in chemistry, must be able to have "a good time by himself, just wondering, and thinking about things, and guessing out as best he can, how they happen." The author disavows any desire to advise men to take up chemistry as a means of support, but he strives to show men engaged in many varied lines of business how a knowledge of the chemistry of the things they handle may be a big asset to them.

He says "a knowledge of chemistry is something like a good wife. It will help a man along in his work, but he must not count on it to support him. We have not yet arrived at the time when chemistry is made as welcome as it should be. It is a good servant but a poor master, except to the man who is himself a master."

The book, which may be easily read in a couple of hours, contains many practical and interesting suggestions, both for the man whose knowledge of chemistry is nil and the one who is more or less familiar with the subject, and is written in a pleasing style.

It is a pity that preparation of copy and proofreading were not more carefully done, so that a number of errors—not very serious, it is true, but errors nevertheless—might have escaped appearing within the covers of the volume. Several of them are here noted.

On page 9, "sulphite (instead of sulphide) of Cadmium" is said



to be "used as a pigment." On pages 10 and 14, Cerium and Thorium, respectively (instead of their oxides), are said to be "used for incandescent gas mantles." On page 42, liquid air is said to be separated "by distilling off first the oxygen, then the nitrogen," when the reverse is the proper procedure, the author apparently overlooked the fact that nitrogen, which he says boils at  $-194^{\circ}$  C., is more volatile than oxygen, the boiling point of which he gives as  $-182^{\circ}$  C. On page 70, alcohol is said to be "a grand solvent for dissolving gums" and "it is an excellent disinfectant." Page 89 contains a statement with reference to the reaction which ensues when calcium phosphide and water are mixed which does not agree with general observations.

F. P. STROUP.

# THE AMERICAN JOURNAL OF PHARMACY

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OCTOBER, 1919

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## EDITORIAL.

### PHARMACEUTICAL RESEARCH.

The following announcement has been issued by the American Drug Manufacturers' Association:

"On August 28 the Scientific Section of the American Drug Manufacturers' Association held a meeting at the Waldorf-Astoria, New York City, at which President Sayre of the A. Ph. A. was a notable guest.

"One of the actions of greatest moment took the form of a recommendation that extracts of aconite leaves be deleted from manufacturers' price lists on the ground that there is practically no demand for these troublesome preparations. In connection with the subject of aconite it was also decided to recommend the recognition of Japanese aconite in the U. S. P., but as a separate drug, since its constituents are somewhat different. It is thought that its admission would relieve the shortage of aconitine, of which there is none available in this country at this time.

"Attention was also given to the fact that some of the menstrua of the U. S. P. are not entirely satisfactory and that, as a result, manufacturers are in many instances obliged to list a formula providing a special menstruum of their own in addition to the formula of the U. S. P., thus multiplying to a degree that is vexatious to both manufacturer and dealer the number of preparations to be carried in stock. With a view to simplification, a subcommittee was appointed to collect the experience of manufacturers on unsatisfactory menstrua and to endeavor to compile a simpler list of menstrua that they will be able to recommend to the Committee of Revision as meeting the approval of all manufacturers.

"If the Executive Committee of the Association adopts a sug-

gestion emanating from Dr. F. R. Eldred of Eli Lilly & Co., the American Drug Manufacturers' Association will take a notable place in the field of fundamental pharmaceutical research. Dr. Eldred proposed that the Association retain the services from time to time of eminent research workers to conduct exhaustive researches on certain drugs of which comparatively little is known and to publish the results of their work for the benefit of all. It was thought that a place might be found for the work in the Mellon Institute and it was remarked that an investigator would progress at an immeasurably faster rate than if working alone since he would have the benefit of the facilities and experience of the laboratories of almost all the pharmaceutical manufacturers of the country. The "Constituents of Digitalis" was suggested as the subject of the first of these treatises for, while the literature of digitalis is voluminous, the subject is left in a most unsatisfactory condition. The section recommended careful consideration of Dr. Eldred's proposal by the Association's Executive Committee."

This is another welcome evidence of the increasing interest that is being manifested on the subject of pharmaceutical research. The pharmaceutical manufacturers who are associated in this organization are in a most favorable position to learn not only of the necessities for scientific investigations and for the broadening of the scope of pharmaceutical research but, likewise, to render valuable assistance in such studies.

Since the development of the industry of manufacturing pharmaceuticals, many valuable contributions to our knowledge of drugs, their actions, constituents, methods of standardizing, and the best forms for exhibition as remedial agents, have emanated from the laboratories of these manufacturers. Many of these resulted from investigations of the problems that arose in the manufacture or marketing of commercial products and so had more or less bearing upon the business with which the investigators were connected. Nevertheless, with the true scientific spirit the information gleaned has been broadly disseminated with only an occasional attempt at reservation for personal advantage. It is especially pleasing to note that an organization such as the American Drug Manufacturers' Association, composed of representatives of firms and corporations that are vitally interested in commercial problems, has assumed such a broad philanthropic attitude and that it is proposed that the research work carried on under its auspices or by its grants shall not



be undertaken for purely commercial reasons but in an altruistic spirit for the service that such investigations may render to science and humanity.

The current issues of the *AMERICAN JOURNAL OF PHARMACY* and of at least several of the other pharmaceutical journals, as well as the past issues, contain many valuable contributions that evidence scientific study and research work and demonstrate that there is no foundation for the heedless criticism that has at times appeared in some quasi-pharmaceutical journals as to a lack of research work in pharmaceutical circles. Nearly every monograph, formula or standard in the U.S.P. or the N.F. is the result of study and in many cases of scientific investigation and pharmaceutical research and contraverts such flippant statements.

The truth is that the field open to pharmaceutical research is of such a wide scope, that the work already accomplished, even though of great magnitude, serves but to present to our view the enormity of the possibilities, the unlimited field of scientific investigations open to pure pharmacy and its collateral sciences that have not yet been made the subject of complete investigations.

We are heartily in accord with the proposition so ably presented in the address of President William Kirby of the British Pharmaceutical Conference, that coöperative research in pharmacy should be undertaken in institutions in which botanical, chemical, pharmacological and bacteriological work can be carried out. In this connection, it is not amiss to direct attention to the fact that at least some of our colleges of pharmacy are well equipped with such departments and the several laboratories essential and are prepared to carry out such coöperative research work, and this should be kept continuously in mind in the selection of subjects and the making of awards for such scientific investigations.

The Mellon Institute has performed valuable service in the making of many able scientific investigations, but it is probably not better equipped to undertake pharmaceutical investigations than are some of our colleges of pharmacy with their laboratories and their libraries of literature pertaining to pharmaceutical subjects and members of their faculties more thoroughly acquainted with the distinct problems of pharmacy and the investigation already made and the methods of pharmaceutical research, and whose students are likewise in a position to render aid by coöperative studies.

The drug trade organizations should not overlook the possibility

of utilizing to the fullest extent the pharmaceutical institutions and the facilities there available for pharmaceutic research. To ignore these would be a serious error and a disregarding of the work already accomplished by pharmacists or now in process and might well be construed as a reflection cast upon the ability of such investigators and the many contributions to science emanating from pharmacists. Conversely, the placing of the responsibility for research work such as is contemplated in the above announcement with pharmaceutical schools should be of material aid to such institutions of learning and redound to the credit and benefit of pharmacy. The very subject suggested for the initial investigation under this patronage, is an excellent illustration of the problems that call for investigation by those who are especially trained as pharmaceutic investigators and acquainted with the existing voluminous literature relating to the subject.

In recent years, much has been written concerning a proposed confederation of all of the drug trade organizations and the pharmaceutical associations in the United States. The discussion and the effort was directed toward a universal coöperation and coördination of all lines of pharmaceutical activities whether intended to cover professional, educational, legislative, commercial or other needs. The diverse interests served by the many drug trade and pharmaceutical organizations precluded the consummation of such a Utopian plan for general coöperation. The objections that were voiced against federation on such a varied line of activities could not apply to the organization of a federation whose prime purpose was to encourage, to stimulate, and to promulgate research study and investigations in pharmacy with the understanding that the results so obtained are to be made public and available to all alike.

Such a federation as here suggested could readily be formed of named delegates from all of the various pharmaceutical and drug trade organizations and would constitute a body under whose direction a comprehensive scheme of research in pharmaceutical subjects could be mapped out and systematically carried on. The title selected might be The American Committee on Pharmaceutical Research, The American Council on Pharmaceutical Research, The American Institute for Pharmaceutical Research, or The American Endowment for Pharmaceutical Research. A portion of the profits accruing from the sale of the U. S. Pharmacopœia and the National Formulary, contributions from the various trade organizations, sup-

plemented by endowments, donations, and bequests from individuals should provide for the financial support of such a research organization that would be truly representative of pharmacy and in an unselfish service perform the great work that would thus be made possible for science and the benefit of the entire world.

Such a plan is needed to make possible any systematic and extensive scheme for pharmaceutical research. The efforts of individual societies in this direction are necessarily restricted and too limited to accomplish very much. At the recent meeting of the American Pharmaceutical Association, the funds available for the Committee on Research would permit of but one award although the Committee had before it several other meritorious requests for allowances for investigations of important subjects that doubtless would likewise have appealed to the members of the American Drug Manufacturers' Association.

G. M. B.

#### DENATURED ALCOHOL REGULATIONS.

The attention of dealers in denatured alcohol is directed to the following instructions and regulation that has been issued by the Bureau of Internal Revenue.

TREASURY DEPARTMENT, OFFICE OF COMMISSIONER OF INTERNAL  
REVENUE, WASHINGTON, D. C.

August 30, 1919.

Non-Bev-Al. Mim. 2248.

*To Collectors of Internal Revenue,  
and Revenue Agents in Charge:*

T. D. 2914 issued today and showing additional matter to be affixed to containers of completely denatured alcohol, is called to your especial attention.

Reports recently received in the bureau establish that completely denatured alcohol is being used extensively for bathing and rubbing purposes. This is contrary to the law and regulations and such uses cannot be tolerated, as the completely denatured alcohol is highly injurious to the skin and animal tissue.

It is also established that completely denatured alcohol is being sold by irresponsible dealers under such circumstances as to assure them that it is being used for beverage purposes. Where it is so



used for any length of time blindness inevitably ensues and the continued use can only result in death.

Collectors should use every means at their disposal to make known to the public the dangers of either external or internal uses of completely denatured alcohol. Wherever collectors or revenue agents in charge hear of a misuse of completely denatured alcohol, a most thorough and careful examination should be made immediately and all the facts fully reported to the commissioner for the infliction upon the responsible parties of the ultimate penalties provided by law.

J. H. CALLAN,  
*Acting Commissioner.*

(Additional matter to be printed on labels affixed to wholesale or retail packages of completely denatured alcohol.)

TREASURY DEPARTMENT, OFFICE OF COMMISSIONER OF INTERNAL  
REVENUE, WASHINGTON, D. C.

*To Internal Revenue Officers and Others Concerned:*

In view of the grave and extended abuses of the use of completely denatured alcohol reported, it is deemed necessary to print upon the labels affixed to wholesale and retail packages a further and more specific warning as to its use than is shown on the present required label.

In addition to the present matter on the labels there will be required on all new labels hereafter the printing in large letters in red ink under the skull and bones symbol, the word: Poison, and at the bottom of the label there will be printed the following statement:

"Completely denatured alcohol is a violent poison. It cannot be applied externally to human or animal tissue without seriously injurious results. It cannot be taken internally without inducing blindness and general physical decay, ultimately resulting in death."

Until the present stocks of labels are exhausted this additional matter may be affixed to the containers on a separate label pasted above the present required label.

J. H. CALLAN,  
*Acting Commissioner.*

Approved August 30, 1919:

CARTER GLASS,  
*Secretary.*

## CHLORETONE: TRI CHLOR TERTIARY BUTYL ALCOHOL. A DESCRIPTION OF SOME OF ITS PROPERTIES.

BY HERBERT C. HAMILTON,  
DETROIT, MICH.

This is a compound formed by the direct union of chloroform and acetone, a reaction which is initiated by a caustic alkali. Willgerodt<sup>1</sup> discovered the reaction in 1881 and produced the compound which he called acetone-chloroform. When purified by steam distillation, or when recrystallized from water, it melts at 80°–81° C., somewhat higher when freed from water by distillation.

*Chemical Properties.*—The empiric formula for chloretone shows it to be apparently a direct combination of chloroform and acetone. Its structural formula, however, indicates that the compound takes on the formation of an alcohol and thus accounts for the chemical designation of tri chlor tertiary butyl alcohol. It is soluble in most organic solvents and oils and is soluble in water—about 0.8 per cent.—from which it crystallizes in slender, white needles.

*Physiological Studies.*—The physiological actions of this compound have been studied by Abel and Aldrich,<sup>2</sup> Kossa,<sup>3</sup> Vamoosy,<sup>4, 5</sup> Houghton and Aldrich<sup>6, 7</sup> demonstrating its action as a local and general anesthetic and as a hypnotic and sedative.

*As a General Anesthetic.*—It has become the general anesthetic of choice for work on laboratory animals, its exceptional value depending upon the fact that it is safe and relatively non-toxic, and that one dose is sufficient to maintain complete anesthesia for several hours uncomplicated by any serious effects on the heart and circulatory system. This applies only to such experimental work as involves an examination of the pharmacologic properties of drug or gland extracts, for example, the standardization of extracts of the suprarenal and pituitary glands where the effect is to raise the blood pressure, study of the digitalis series of heart tonics which affect primarily the circulatory system, of aconite and veratrum which are circulatory depressants, of blood coagulants which act to decrease the time of blood clotting.

For operations in which the recovery of the patient is of first importance, chloretone can be used in conjunction with morphine by which complete anesthesia can be accomplished using a sublethal

dose of the chloretone but a dose large enough to prolong the anesthesia over a period of several hours. The technic for such work has been well described by Rowe,<sup>8</sup> for while there is no difficulty involved, attempts to apply this method of anesthesia have not always been successful.

*As a Hypnotic and Sedative.*—Another very common use made of chloretone is to allay the nausea due to seasickness. This is probably brought about, not only by the sedative and anesthetic action of the drug on the stomach lining, but also by the general action on the central nervous system. Autopsies show that more chloretone is found in the brain than in any other organ of the body, which is a logical finding in view of its exceptional efficiency as a general anesthetic. While it is a highly volatile product, it appears not to be eliminated by the lungs nor as such, in the urine, but is finally decomposed as shown by an increase in the chlorides. Chloretone is regarded by the medical profession as producing the closest approximation to natural sleep that has yet been discovered, in its safety and reliability and in the fact that no unpleasant after effects are experienced. The substance is carried to the cerebral tissue and profound sleep occurs. After a time as the chloretone is gradually broken up and carried away chemical activity is renewed in the brain cells and the patient awakes, refreshed as from natural sleep.

The mode of administration seems to have little influence on its absorption, for animals kept in an atmosphere saturated with vaporized chloretone are anesthetized, in time almost as completely as if it were administered internally.

*Insecticidal Action.*—This action of the vapor suggested its use as a substitute for naphthalene as an insecticide for clothes moths. Experiments were carried out on moths, flies and mosquitos which showed that for the latter insect chloretone is four times as effective as sulphur fumes and almost as effective as the latter for moths and flies. It is as effective for moths as naphthalene without the objectionable odor of the latter.<sup>9</sup>

In these experiments weighed quantities of the substance were vaporized in a bell jar or in a laboratory hood of known capacity and the condition of the insects or animals carefully noted. It requires four or five hours to anesthetize guinea pigs and it is necessary to volatilize the chloretone slowly, carrying the vapors in with a current of air. For insects which require less air the rapid volatilization in a short time is somewhat more effective than the slower method because of its prompt action.



*As a Local Anesthetic.*—When chloretone is tested by some of the laboratory methods used for comparing local anesthetics it is found to be surprisingly effective. Tested on the sciatic nerve of the frog one of the standard methods applied for substances of this character and compared to cocaine the results are as follows:

*Chloretone.*

	0 Min.	5 Min.	10 Min.	15 Min.	20 Min.
0.8 per cent. solution.....	—	±	+	+	+
0.4 per cent. solution.....	—	—	+	+	±
0.2 per cent. solution.....	—	—	—	±	±

*Cocaine.*

1 per cent. solution .....	—	±	+		
0.5 per cent. solution.....	—	±	+		

Another test applied to local anesthetics is to measure the anesthetic action on the frog's skin. This is always moist and is comparable to the mucous membrane. The test is carried out by dipping one leg of the frog into the solution to be tested, leaving the other undipped as a normal for control. After contact for a determined time both legs are dipped into a very dilute solution of HCl—about 1-500. Anesthesia can be measured by finding the maximum dilution which is effective and comparing with a solution of cocaine of equal activity. The following results were obtained:

*Chloretone.*

Minutes.	0.8 Per Cent. Solution.	0.4 Per Cent. Solution.	0.2 Per Cent. Solution.
0	—	—	—
2	+	+	—
5	+	+	±
8	+	+	—
10	+	±	—
15	+	—	—

*Cocaine.*

Minutes.	1 Per Cent. Solution.	0.5 Per Cent. Solution.	0.25 Per Cent. Solution.
0	—	—	—
2	—	—	—
5	±	±	—
8	±	±	±
10	+	+	±
15	+	±	—

*Note.*—Minus, —, no anesthesia. Plus, +, complete anesthesia. Plus minus, ±, partial anesthesia.

As an anesthetic for the mucous membrane, therefore, it is even better than cocaine, and in its direct action on the exposed nerve as on the sciatic nerve, the anesthesia is as prompt and as lasting as that of cocaine.

It fails, however, to replace cocaine because of its low solubility. It is precipitated in the tissues and is rather irritating and ineffective on that account. Its local action on the sense of taste is shown by the fact that its rather bitter disagreeable taste is only momentary in the mouth but when the solution reaches the throat the objectionable taste is again evident.

Aside from the wide applicability of chloretone as a general anesthetic, its most valuable property is as a germicide and antiseptic, the properties essential in a preservative. If the "bone-dry" legislation keeps on, chloretone will be one of the few preservatives left for organic medicinals.

*Germicidal.*—As a germicide it has a phenol coefficient of 1.2, that is, when tested by the Hygienic Laboratory method of evaluating disinfectants it is as effective in 0.8 per cent. solution or 1-120, as phenol diluted 1 in 100, that is, a culture of *B. typhosus* is killed when exposed to the action of either of these two disinfectants for two minutes.

Tests by the A. P. H. A. Phenol Coefficient method<sup>10</sup> are given for chloretone and phenol.

For an antiseptic test the two latter organisms were inoculated in medium saturated with chloretone. In no case was growth observed over a period of three weeks. Tested against other more resistant organisms it is found that in most cases to be effective it requires a longer time than a disinfectant can be expected to act and therefore that it must be classed as a preservative or antiseptic rather than a germicide. For this purpose, with but few exceptions, it is ideal; even the highly resistant hay bacillus, *B. subtilis*, fails to develop in a solution saturated with chloretone. In some instances where the solution is an exceptionally good medium for the growth of bacteria it requires more than 4 days to become sterile, but evidence of growth is not apparent. It is absolutely essential that the container be closed against the volatilization of the chloretone and a full container is advisable because of the tendency of chloretone to crystallize on the walls above the solution. This may be due to supersaturation but if so it is a condition to be retained if possible.

GERMICIDAL EXPERIMENTS.

*Typical Test of Phenol.*

Dilution.	Time and Results, Minutes,			
	5.	10.	15.	20.
1-100. ....	—	—	—	—
1-110. ....	+	—	—	—
1-120. ....	+	+	—	—
1-130. ....	+	+	+	—
1-140. ....	+	+	+	+

*Test of Chloretone.*

*Saturated Aqueous Solution. (B. Typhosus.)*

Dilutions.	Time and Results, Minutes.			
	5.	10.	15.	20.
5 cc. 0.8 per cent. sol. + 0 cc. water ....	—	—	—	—
9 cc. 0.8 per cent. sol. + 1 cc. water ....	+	+	—	—
8 cc. 0.8 per cent. sol. + 2 cc. water ....	+	+	+	+
7 cc. 0.8 per cent. sol. + 3 cc. water ....	+	+	+	+
6 cc. 0.8 per cent. sol. + 4 cc. water ....	+	+	+	+

+ means growth.

— means no growth in subculture.

*Staphylococcus.*

	5 Min.	10 Min.	15 Min.	20 Min.
0.8 per cent. solution .....	+	+	+	+

*Spores of Hay Bacillus. (B. Subtilis.)*

	1 Hr.	2 Hr.	3 Hr.	4 Hr.
0.8 per cent. solution .....	+	+	+	+

*Mould Spores.*

	1 Hr.	2 Hr.	3 Hr.	4 Hr.
0.8 per cent. solution .....	+	+	+	+

Such a solution can be obtained by adding the chloretone in a saturated alcoholic solution, by heating the chloretone in water, or by allowing several days for complete saturation.

As a preservative against mould spores it has not proved entirely satisfactory for serums and heavy organic solutions. The strains used in this experimental work have, however, invariably



failed to develop in an agar-bouillon medium but in practice moulds occasionally appear showing either loss of chloretone through volatilization or the presence of a more resistant variety. It seems probable that the occasional development of mould in pharmaceutical preparations preserved with this agent is due to a deficiency of the agent rather than a more highly resistant mould because of failure to obtain a saturated solution or a decrease in the chloretone content from other causes.

It is the purpose of this paper to emphasize two of the properties of chloretone which seem to be exceptionally valuable and which should commend it to laboratory purposes. First, as a general anesthetic for animal experimentation, it has no equal because of its long-continued action and non-interference with the circulatory system. Second, as a preservative where its antiseptic and germicidal action can be relied upon to prevent the development of bacteria and ultimately to kill the organisms which not only impair the appearance, but also destroy the valuable properties of organic solutions. It can be used in many cases where the preservative action of alcohol must be eliminated and especially where sterilization by heat is impracticable because of its destructive action on sensitive organic compounds.

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1911. *J. A. P. H. A.*, 1, 227.
10. Committee Report, *J. A. P. H. A.*, July, 1918.  
FROM THE RESEARCH LABORATORY,  
PARKE DAVIS & Co.,  
DETROIT, MICH.

## A REVIEW OF THE ADVANCES IN PHARMACY.

BY JOHN K. THUM, PH.M.,

THE LANKENAU HOSPITAL, PHILADELPHIA.

*The Decimal System in Trade.*—Under the caption "Banish the Dozen System" the *Philadelphia Public Ledger* in a recent issue strongly advocates the use of the decimal system in trade. The drug trade in its advocacy of the metric system has always laid great stress on the fact that our money system is based on the decimal; this newspaper also brings out this argument to buttress its plea. We consider this editorial so peculiarly apropos that we would feel ourselves remiss in our duty to the profession if we failed to quote this timely article:

"One of these fine days a person may go to a store and ask for a dozen eggs and be told eggs and other things no longer are sold by the dozen but by the decimal system.

"And why shouldn't they be sold that way? America has the decimal money system. It should not have another in trade.

"There is as much confusion in the systems of weights and measures as there is confusion in languages. The British have a 'stone' and a quarter. How many Americans know what these terms signify? The British also have a farthing, a penny (which is equal to our two cents), a sovereign, a pound, a guinea and other measurements of money.

"No system is so simple as the decimal. This fact is being appreciated by business men. The rubber companies of America have adopted it. One of them, writing to the secretary of commerce, says:

"We will not claim the honor of being the exact pioneer in this movement, as it was agreed among all rubber companies hereafter to price everything in the unit system, and our factory adopted the 100-unit as a price basis. This reduces at once the cost of a single article by moving the decimal point two figures or, in other words, you have the price of each piece of goods in a single unit at a glance.

"The Department of Commerce, in an investigation it has made, finds the decimal gives satisfaction and minimizes mistakes, as units of 10, 50 and 100 are more easily accounted for than dozens, and the gross, which is a dozen dozen. The company whose report is quoted packs its goods in lots of ten, twenty-five, fifty and 100.

"The department quotes a knitting company of California, which says it 'feels certain that many weary-brain hours could be saved by the elimination of the dozen unit, as this also involves the translation of price from dozen to single pieces, or a division by twelve.'

"Banish the dozen."

*What is a Pharmacist?*—In the *Chemist and Druggist* of May 10 the foregoing question is asked and then answered in a quotation from Edward R. Squibb, which deserves to and probably will go down to pharmaceutical posterity as a classic: "A pharmacist is not a druggist. A druggist is a merchant of drugs, a dealer in substances which, though originally used in medicines, came to be used in many other arts. The pharmacist, synonymous with pharmaceutist and apothecary, but not with druggist or chemist, is an educated, qualified practitioner of the art of pharmacy. He is a dealer in substances used to prevent and relieve distress; who has the knowledge and skill to secure a proper quality in his merchandise; to prepare this for its ultimate uses; and to secure it against accident and criminal misapplication. The druggist is a merchant like the grocer, the dry-goods dealer, etc. The pharmacist may be all this, but must be very much more."

*A National Department of Health.*—Hon. Joseph I. France, United States Senator from Maryland and chairman of the Senate Committee on Public Health and National Quarantine, has introduced in the senate a bill with the above title which covers the subject in a very broad way. This makes the third bill now before Congress, a fact which shows clearly that the need and usefulness of an efficient national department of health is becoming more apparent every year and especially since our entrance into the Great War. The result of the physical examination of many of our draft recruits, a rejection of nearly 29 per cent., is a good argument for showing the necessity of the government taking an intelligent and active interest in the health of its people, and the conditions and environment that promote health and general well-being. For instance, what a tremendously important thing it is for the people to know something about the need of proper care of public water supplies and proper disposal of excreta, especially in the rural sections of our country. This matter could be more readily pressed home to the people if planned on a national scale with the full force and power of the government supporting it.



The bill, which is called Senate Bill 2507, provides for a department of public health under the direction of a secretary, who is made a member of the cabinet, and three assistant secretaries, the first assistant to be a man with medical training, with knowledge of public health measures, including sanitation; the second to be thoroughly grounded in vital statistics; and the third to be a woman trained in medicine or nursing and public health. It is proposed in the bill that the U. S. Public Health Service and Bureau of Chemistry be placed under the jurisdiction of the department, which is also to have a bureau of vital statistics, sanitation, hospitals, child and school hygiene, quarantine, food and drugs, nursing, tuberculosis and personnel. The secretary of public health is directed to communicate with the governor of each state requesting him to recommend to the state assembly suitable legislation with sufficient appropriation of money to secure coöperation between the federal department of public health and the state board of health. Every state taking such action will be entitled to a proportionate share of such money as may be appropriated by Congress for carrying out the provisions of this act. The bill provides for the division of the country into health states, districts, subdivisions and precincts, each conforming to the geographical boundaries of the various political divisions. The bill also provides for coöperation with the Departments of Commerce, Labor and the Interior in the collection of vital statistics and to establish a uniform system of cards, records and reports regarding diseases, disabilities, industrial accidents, births, deaths, physical condition of school children, the number and conditions of existing hospitals, etc. The bill provides for an appropriation of \$15,000,000 for 1920 to be divided among those states, in proportion to their population, who comply with the requirements of the law and likewise appropriate a sum equal to the federal contribution, and make full and complete reports of deaths, births, etc. An appropriation of \$48,000,000 is made for the erection of sanatoriums and hospitals, to be divided among the various states in proportion to their population, each state of course contributing an equal amount. Undoubtedly the time seems ripe for the inauguration of a comprehensive plan for looking after and safeguarding the public health from every standpoint. Certainly human rights should be regarded by the Government as being at least on a par with property rights. A healthy people is a nation's most important

asset. "Lest we forget" let us bear in mind the terrible time of the "flu" last year.

*Rapp's Method for the Estimation of Alkaloids.*—It is claimed that this method gives very satisfactory results, but it is necessary that the amount of plaster of Paris added should be just sufficient to prevent the mixture from hardening, in fact a soft paste-like mixture answers very well. A preliminary blank trial with the plaster to be used is desirable. In the original method it is desirable to make sure by an extra shaking with 10 mls of chloroform that all the alkaloid has been extracted from the mass. Uncertainty may be avoided by dissolving the alkaloid first with chloroform before the addition of the plaster and then proceeding with an aliquot portion of the filtered extract for the estimation. As an example, in the determination of cinchona bark, the substance is treated with the quantity of liquid advised by Rapp and then agitated in the same flask with 50 mls of chloroform, made alkaline, and shaken with 25 grams of plaster of Paris. The chloroform is then filtered off and the filtrate shaken with tenth-normal acid. The plaster paste in this case may be of any degree of stiffness, as it does not have to be washed out, all the alkaloid having been dissolved by the chloroform previous to the addition of the plaster. In view of the excellent results obtained it is suggested that the principle of Rapp's method be applied to other extraction operations besides those with alkaloids, as the use of plaster has a clarifying effect and assists the separation of the extract.—*J. Pharm. Chim.*, 1919, 19, 295, through *The Analyst*, July, 1919, page 236.

*Iodine Value (Wijs) of Palm Kernel Oil.*—The normal range of iodine values for palm kernel oil is 16 to 23. The average value for 574 samples of refined oil was found to be 18.1, and for 1,236 samples of crude oil 18.6. The oils worked with in this investigation were expressed from the kernels crushed in the mill under ordinary works conditions.—*J. Soc. Chem. Ind.*, 1919, 38, 128, through *The Analyst*, July, 1919, page 237.

*Analysis of Prune Kernels.*—Prune kernels gave a yield of 42 per cent. of oil, 2.47 per cent. of nitrogen, and 37.42 per cent. of sugars. When cooled to 5° C. the oil partially solidified, the solid portion being about one third of the whole amount. The sp. gr. of

the solid part being 0.9055, the saponification value 239.8; the liquid portion had a sp. gr. 0.9119, and saponification value of 207.4. The sugars found present were lævulose, dextrose, and possibly cane sugar.—*Chem. News*, 1919, 118, 242–243, through *The Analyst*, July, 1919, page 238.

*Estimation of Lactose and Proteins in Milk Preserved with Potassium Dichromate.*—Polarimetric estimation of lactose in milk containing this chemical as a preservative is unreliable, as the quantity of sugar found decreases gradually until after about 70 days only 50 per cent. of the amount originally present is obtained. However, the quantity of lactose does not show any decrease during this period, when it is estimated by determining its copper-reducing activity. Casein also shows considerable change; while the quantity of total protein remains the same, the casein (protein precipitated by acetic acid) decreases 2.58 to 2.10 per cent. in 40 days.—*Ann. Falsific.*, 1919, 11, 78–79, through *The Analyst*, July, 1919, page 237.

*Oil of Ceratotherca sesamoids.*—The plant is allied to *Sesamum indicum* (Gingelly), and the specimen investigated came from the Gold Coast, and is known in that region under the name “Bungu.”

The seeds are similar to the white *Sesamum indicum* in general appearance, somewhat reddish brown in color and larger than the latter, 100 seeds weighing 0.34 and 0.24 respectively. The seeds are more flat than *Sesamum indicum*, and the edges are darker in color than the rest of the seed and have a serrated appearance.

On extracting the ground seed with petroleum ether there was obtained 35.47 per cent. of a pale yellow oil with a slight nutty flavor. On standing there was precipitated some “stearine.”

The following analytical figures were obtained for the oil:

Saponification value .....	190.20
Unsaponifiable matter .....	1.53%
Iodine value .....	110.60
Refractive index at 40° C., zeiss. ....	59.60
Free fatty acids (as oleic) .....	0.63%
Specific gravity 15° C. ....	0.9163
Baudouin reaction .....	negative.
Halphen reaction .....	negative.

That the Baudouin test, which is such a delicate color reaction for *Sesamum indicum*, should prove negative is noteworthy, in view



of the fact that this plant is so closely related to *Sesamum indicum*. One would expect it to be otherwise, as in the case of the Halphen test for cottonseed oil, which is also given by Kapok oil, the plant from which this oil is obtained being closely related to the cotton plant.

The other results obtained with this oil are within the limits for sesamé oil, although the specific gravity is somewhat lower.

The oil is edible, and could be made of use in the manufacture of margarine, etc., if the seed were obtainable in large enough quantities. Its low free fatty acid content and relatively slight taste should make it available for the preparation of edible oils.—*The Analyst*, July, 1919, page 233, E. Richards Bolton.

*Reaction of Aconitine*.—The red color, mentioned by Dragen-dorff as characteristic of this alkaloid, produced when aconitine is heated with phosphoric acid, is usually only obtained with amorphous products. The pure crystalline aconitine heated with phosphoric acid (sp. gr. 1.7) yields only a faint gray color. By using a mixture of the acid (25 grams) and sodium molybdate (1 gram), a brilliant violet coloration is produced with samples of crystalline aconitine which give no color with phosphoric acid alone. Of the other common alkaloids the only ones that give color reactions that could be mistaken for the aconitine reaction are aspidospermine (deep violet) and veratrine (violet red). The first may be differentiated from aconitine by the action of oxidizing agents, and the other by the action of mineral acids.—*J. Pharm. Chim.*, 1919, 19, 295–296. L. P. J. Palet, through *The Analyst*, July, 1919, page 236.

*Influence of Various Ammonium Salts on the Precipitation of Magnesium Hydroxide*.—The writer of this paper shows that the sulphate of ammonium is rather more effective than the chloride in holding up magnesium hydroxide. This fact does not agree with the theory given in many text-books to explain the mechanism of the hindrance that ammonium salts have on the precipitation of magnesium salts. Unsuccessful attempts were made to apply this knowledge to the separation of calcium and magnesium. Aside from the fact, in presence of sulphates, solutions of calcium salts must be highly diluted, which is inconvenient, the writer has failed to obtain exact or even concordant results.—*Helv. Chim. Acta*, 1919, 2, 277, through *The Analyst*, July, 1919, page 245.

## PHARMACY IN THE ARMY AND NAVY DISCUSSED BY THE N. P. S. A.

A meeting of the National Pharmaceutical Service Association was held on the evening of August 28 at the Hotel Pennsylvania, during the Convention of the American Pharmaceutical Association, and everyone was cordially invited to be present.

The President, Dr. Frank Cain of Cincinnati, presided, and read an address urging the joint effort of pharmaceutical organizations, working in harmony with physicians toward the proper recognition of pharmacy in the Army and Navy. He also presented the following letter from the Surgeon-General, which was received with applause and recognized as the beginning of the cordial relationship which will undoubtedly result in the adequate recognition of pharmacy:

WAR DEPARTMENT  
OFFICE OF THE SURGEON-GENERAL  
WASHINGTON

August 14, 1919.

PROFESSOR E. FULLERTON COOK,  
145 North Tenth Street,  
Philadelphia, Pa.

*My dear Dr. Cook:* I now desire to give you in writing the substance of the observation we had on August 11, in regard to commissions for pharmacists in the medical department of the Army. I think it is most important for the future welfare of the medical department to have a service corps for commissioned officers. To become an officer in this corps, it will be necessary for an applicant to enlist in the medical department and serve for a period of about five years. During this time he will be given an opportunity to perfect himself in hospital administration, quartermaster's duties, motor transport service, mess management, registrar's duties, pharmaceutical work, and the general duties of the hospital corps. It will be one of the requirements that an applicant for a commission in the service shall be a non-commissioned officer for three years of his five-year enlistment. The duties of the officers of the service corps will be to act as adjutants of our large hospitals, property officers, mess officers, transport officers for the ambulance companies, and various other duties of non-professional character, connected with the medical department, for which we now have to use a highly trained medical officer.

I have recommended to the General Staff that a service corps for the medical department be incorporated in the army reorganization bill now before Congress, and I sincerely trust this corps will be authorized.

I am perfectly willing that a limited number of vacancies in the service corps shall be set aside for men who specially qualify themselves as pharma-

cists, and in the course of instruction which candidates for the service corps will have to take, suitable provision will be made for advanced instruction in pharmaceutical work.

After our very frank discussion of the needs of the medical department for pharmacists, I think we both agree that this will solve the question in a most satisfactory manner.

With cordial regards, believe me

Very sincerely yours,

(Signed) M. W. IRELAND,

*Surgeon-General, U. S. Army.*

The President believed that the proposal of the Surgeon-General should be carefully considered and that a conference should be held with the Surgeon-General by a committee representing the several pharmaceutical organizations, and by this means to arrive at a plan whereby the association can assist the Surgeon-General in his effort to establish a "service corps" and also provide a better status for pharmacists in the corps.

It was believed that the five years of non-commissioned service as a prerequisite to commissions should be modified for those men who have adequate scientific training, although the Surgeon-General's desire that the candidate for commission should have thorough military training was recognized as essential.

The Secretary presented a statement of the general situation in both the army and navy, calling attention to the fact that the Hospital Corps Bill known as H. R. 4760 has been combined in what was known as the Personnel Bill, and hearings will be granted some time this fall. The importance of securing the approval of the Secretary of the Navy was emphasized, and since then it has been learned that this will be of vital importance in obtaining the favorable consideration of the Naval Affairs Committee. Every effort should be made to enlist the interest and secure the approval of Secretary Daniels.

Colonel Frederick M. Hartsock, of the Surgeon-General's office, was present and spoke of the excellent work done by pharmacists in the Army, which was recognized as indispensable. He said the general staff had not yet worked out the details of the reorganized army, but that pharmacy should, in his opinion, be given adequate recognition. He recommended that proper presentation be made by pharmacists of their cause and that a definite plan be worked out and presented to the Surgeon-General. A vote of thanks was extended to Colonel Hartsock for his frank statement and evident interest in pharmacists in the service.



Mr. Beringer, in expressing appreciation for the statement made by Colonel Hartsock, expressed the hope that Colonel Hartsock would take back to the Surgeon-General's office the sense of this meeting and of this Association, which had always stood for co-operation with the Surgeon-General and whose desire was to give the army and the navy the most efficient aid and trained service which pharmacy could offer and only asked for an opportunity on a basis which would permit the best service.

Lieutenant W. T. Minnick, of the Hospital Corps of the Navy, then spoke of the work of the pharmacist in the navy. He stated that a Surgeon-General is compelled to take the view of the best interests of the entire service in recommending a preliminary military training before receiving commissions. He explained the many activities of the pharmacist in the navy and the need for thorough training. The Association voted a motion of thanks to Lieutenant Minnick for his clear exposition of the situation in the navy.

Mr. Charles F. Harding, President of the National Association of Retail Druggists, was present and promised the coöperation of the N. A. R. D. in every proper effort which would be started to insure proper recognition of pharmacy in the army and navy, and he suggested that all interests get together in a conference and devise a plan upon which all could unite. In the limited time available, the general subject was discussed by Professor Spease of Cleveland, Mr. Mayo of Cincinnati, Captain MacCartney, a pharmacist who served in the department of supplies in the Surgeon-General's office throughout the war, and by others.

Mr. Beringer moved that a committee be appointed by the President to endeavor to secure an early conference with the Surgeon-General of the Army, if possible in coöperation with similar committees from other national pharmaceutical associations, presenting the views of American pharmacy concerning the Surgeon-General's suggestion for the organization of a "service corps," and the recognition of pharmacy as set forth in his letter of August 14, endeavoring to arrive at a mutually satisfactory plan for the establishment of pharmacy in the army. This motion was seconded and unanimously approved. Dr. Cain, the President, appointed on this committee for the conference with the Surgeon-General of the Army, Mr. George M. Beringer, chairman, and Mr. Caswell A. Mayo and Mr. E. Fullerton Cook as the other members.

SUMMARY OF THE PROCEEDINGS OF THE TWENTIETH  
ANNUAL MEETING OF THE AMERICAN CONFER-  
ENCE OF PHARMACEUTICAL FACULTIES.

PREPARED BY THEODORE J. BRADLEY,

*Secretary.*

The twentieth annual meeting of the American Conference of Pharmaceutical Faculties was held at the Hotel Pennsylvania, New York City, on August 25-26, 1919. Delegates were in attendance from about thirty colleges located in twenty-four states. The President, Dean Charles B. Jordan of Purdue University School of Pharmacy, Lafayette, Indiana, presided at all sessions and his presidential address was one of the features of the meeting. Of the constructive recommendations made by the President, the following were adopted after consideration and report by a special committee on the address:

1. That the dues be increased from ten dollars to twenty-five dollars per year for each member college, and that the entrance fee shall be twenty-five dollars hereafter.

2. That the Executive Committee prepare a budget showing the amounts that can properly be expended by the standing and other committees of the Conference for expense.

3. That the Executive Committee take steps to have the Conference coöperate with other organizations to suitably memorialize the service rendered by pharmacists in the Great War.

4. That the Conference approve the exchange of lectures between members of the faculties of member colleges.

5. That a special committee be appointed to prepare a memorial to the Carnegie Foundation, requesting that an investigation be made of pharmaceutical education in the United States, similar to the investigations already made of medical education, dental education, etc.

6. That the Conference appoint a special committee to collect and distribute information on prerequisite legislation to aid in the securing of such legislation in states not yet having a prerequisite in pharmacy, this committee to act jointly with a similar committee of the National Association of Boards of Pharmacy.

7. That the Conference reaffirm its adoption of high school graduation as a requirement for entrance to all member colleges

after July 1, 1923, and to recommend that this entrance requirement be made effective at an earlier date when possible.

The Secretary-Treasurer, Theodore J. Bradley of Massachusetts, presented his report, in which the President's recommendation that the dues in the Conference be increased was endorsed. The total receipts of the Conference for the past year amounted to \$492.66 while the expenditures were \$863.72, the deficit being made up from the accumulated balance in the treasury. The balance on hand July 31, 1919, was \$686.27, of which \$600 is invested in Liberty Bonds.

Reports of the various standing and special committees were received as follows:

- Executive Committee, J. A. Koch of Pennsylvania, Chairman;
- National Syllabus Committee, T. J. Bradley of Massachusetts, Chairman;
- Committee on Higher Educational Standards, W. J. Teeters of Iowa, Chairman;
- Committee on Faculties, Zada M. Cooper of Iowa, Chairman;
- Committee on Curricula and Teaching Methods, J. W. Sturmer of Pennsylvania, Chairman;
- Committee on Activities of Students and Alumni, R. A. Lyman of Nebraska, Chairman;
- Committee on Relations of Pharmacy Schools and Other Professional Schools, W. F. Rudd of Virginia, Chairman;
- Committee on Research, Henry Kraemer of Michigan, Chairman;
- Committee to Consider and Report on the Question of the Establishment of Two Classes of Pharmacists and Corresponding Courses in Colleges of Pharmacy, Jacob Diner of New York, Chairman;
- Committee to Work out Methods of Presenting the Advantages of Pharmacy as a Calling to High School Students, W. B. Day of Illinois, Chairman;
- Joint Committee on Examination Questions, E. A. Ruddiman of Tennessee, Chairman;
- Committee on Relation of the Colleges with the Boards, Charles E. Caspari of Missouri, Chairman.

All of these committee reports will be published in the Proceedings of the Conference and several of them will appear in other publications.

H. H. Rusby of New York read a paper on the Betterment of Salary Conditions in our Schools of Pharmacy, and, after discus-



sion, it was voted that the Executive Committee send copies of this paper to the administrative heads of all colleges of pharmacy with the request that steps be taken to secure additional funds so that the salaries paid to teachers in the pharmacy school can be materially increased.

W. H. Ziegler of South Carolina presented a paper on the teaching of pharmacodynamics and related subjects in pharmacy schools, which was thoroughly discussed by many of the delegates present.

It was voted to appoint a representative for the Conference on the newly organized pharmaceutical publicity committee, representing all the interests allied with pharmacy and to pay its share of the expenses of this Committee.

It was voted to accept the invitation for the Conference to be represented in the National Drug Trade Conference.

The following officers were elected for the ensuing year:

President: Wortley F. Rudd of Richmond, Va.

Vice-President: Julius A. Koch of Pittsburgh, Pa.

Secretary-Treasurer: Theodore J. Bradley of Boston, Mass.

Chairman of the Executive Committee: Henry Kraemer of Ann Arbor, Mich.

Members of the Executive Committee: Charles B. Jordan of Lafayette, Ind., Julius W. Sturmer of Philadelphia, Pa., Rufus A. Lyman of Lincoln, Neb.

Member of the Pharmaceutical Syllabus Committee, E. Fullerton Cook of Philadelphia, Pa.

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## THE DETECTION AND ESTIMATION OF COCAINE, HEROINE, AND VERONAL IN VISCERA.<sup>1</sup>

BY P. A. ELLIS RICHARDS, F.I.C.

The viscera usually examined in cases of suspected narcotic poisoning are the liver, spleen, kidney, brain, stomach, and intestines, together with the contents of the last two, the urine, and, occasionally, the blood. In cases where a portion only of any organ, such as the liver, is submitted, the total weight of the latter should be ascertained from the pathologist carrying out the post-mortem examination, in order that in the event of a poison being found the

<sup>1</sup> Reprinted from *The Analyst*, June, 1919.

quantity present in the whole organ may be calculated. The same remark naturally applies to the urine when a portion only has been reserved for analysis.

The various organs and fluids are weighed, and the former reduced to a suitable state of subdivision. This is best effected, after a little preliminary dissection, by passing the material twice through a mincing machine, when aliquot portions can be taken for analysis. At this stage it should not be forgotten that, although medical evidence may have suggested death from a narcotic, the analyst in most cases must satisfy himself that no other poison is present.

A weighed portion of the material, acidulated with tartaric acid, should in the first place be distilled in a current of steam and the distillate reserved for examination with a view to the detection of volatile poisons—*e.g.*, chloral, chloroform, etc.

A further weighed quantity of viscera, rendered acid with acetic acid, is warmed with double its volume of alcohol (90 to 95 per cent.), allowed to stand for some hours, the alcohol decanted, and the residue again extracted with the same solvent. The various portions of alcohol are mixed and filtered through cloth, using the filter pump if necessary, concentrated, and again filtered—this time through paper. If the solution be still too deeply colored, lead acetate may be used as a clearing agent, the liquid being again raised to the boiling-point, filtered, and the lead removed by hydrogen sulphide. The filtrate, after concentration to small bulk at a low temperature, is reserved for the extraction of alkaloids, veronal, etc.

The urine, rendered faintly acid with acetic acid, is raised to the boiling-point, allowed to simmer, small portions of finely powdered lead acetate being added from time to time until precipitation ceases. After filtration and removal of the lead by hydrogen sulphide the liquid is concentrated to small bulk and reserved for examination as before.

Each of the various concentrations acidulated with acetic acid is extracted in a separate funnel with successive small quantities of ether. The various portions of solvent are mixed, the ether evaporated, the residue, if any, dried in the water-oven, weighed and examined for veronal, sulphonal, trional, etc.

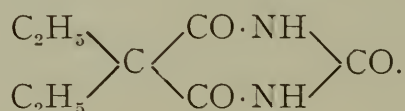
The aqueous solution, after the ethereal extraction just described, is rendered alkaline with ammonia and shaken with chloroform, this operation being repeated three times, the various portions of the

solvent mixed and shaken with two successive portions (10 Cc.) of  $\frac{N}{10}$  hydrochloric acid. The aqueous solution, after rendering alkaline with ammonia, is reextracted with chloroform. The residue obtained after distilling off the chloroform may, where cocaine is suspected, be reextracted with benzene, in which this alkaloid is distinctly soluble.

The final residues obtained are dried, weighed, redissolved in suitable solvents, and aliquot portions evaporated in small flat-bottomed porcelain basins. One residue in each case is treated with a few drops of a 2 per cent. acetic acid solution and the special alkaloidal group-tests applied, the precipitates, if any, being reserved for microscopical examination and comparison with those obtained from known alkaloids.

The following notes on the identification of certain narcotics may be of interest:

*Veronal* (B.P. Barbitone, Diethyl barbituric acid).



This is a white crystalline substance with a slightly bitter taste, sparingly soluble in water (1 part in 150), and, when pure, has a melting-point of 191° C. After extraction from viscera the melting-point is frequently slightly lower, about 186° C. The medicinal dose given in the B.P. is 5 to 10 grains, whilst it is suggested by W. H. Willcox that 50 grains may be regarded as the minimum fatal dose for a healthy adult.

In cases of death from veronal poisoning the organs frequently contain a fair amount of the substance, and, as the latter is excreted by the kidneys, one usually finds a distinct proportion in the urine. Sometimes, however, a considerable period elapses between the taking of the fatal dose and the resulting death, and under such circumstances much of the drug may have been eliminated.

Veronal dissolves very rapidly in alkaline solutions and is easily extracted from an acid solution by means of ether. The crystalline character of the ethereal extract is to help in its detection, as also is the melting-point and the fact that it sublimes completely if carefully heated. The crystalline sublimate, if any, yielded by the extract may be compared microscopically with that obtained from



actual veronal. Confirmation of the presence of veronal may be obtained by adding a small portion of the extract to a little fused potassium hydroxide, when ammonia should be evolved and the residue yield effervescence of carbon dioxide and a curious fatty odour on treatment with dilute sulphuric acid. The Prussian-blue test with ferrous sulphate and the pink color with copper sulphate mentioned in the B.P. are not so satisfactory in toxicological tests. Millon's reagent (mercury dissolved in dilute nitric acid) gives a white gelatinous precipitate which dissolves in excess of the reagent.

Ammoniacal copper sulphate + veronal evaporated to dryness on a microscope slide gives pink to violet crystals that are fairly definite when compared with control slides (Tunmann, *Apoth. Zeit.*, 1917, 32, 289-299; and *Analyst*, 1918, 43, 67). I find that a solution of veronal in dilute ammonia, when evaporated, yields long crystals with serrated edges, markedly differing from those yielded by trional and sulphonal under the same conditions.

*Sulphonal*,  $(\text{CH}_3)_2\text{C}(\text{C}_2\text{H}_5\text{SO}_2)_2$ ;

*Trional*,  $\text{CH}_3\text{C}_2\text{H}_5\text{C}(\text{C}_2\text{H}_5\text{SO}_2)_2$ ;

*Tetronal*,  $(\text{C}_2\text{H}_5)_2\text{C}(\text{C}_2\text{H}_5\text{SO}_2)_2$ .

These are all white crystalline substances of similar type and reactions, and are much less toxic than veronal, being frequently employed as hypnotics. The B.P. gives the doses as from 10 to 20 grains for trional and tetronal, and from 10 to 30 grains for sulphonal, whilst considerably larger amounts would be required to produce fatal results.

They are best identified by their melting-points, these being: sulphonal,  $125^\circ \text{C}$ .; trional,  $75^\circ \text{C}$ .; and tetronal,  $85^\circ \text{C}$ . As a class these sulphones are sparingly soluble in water, but much more so in alcohol. When heated strongly they yield sulphur dioxide, with fused potassium cyanide they give an odor of mercaptan, whilst with fused sodium acetate they evolve hydrogen sulphide.

*Heroine*, di-acetyl morphine,  $\text{C}_{21}\text{N}_{23}\text{NO}_5$ , formed by the action of acetic anhydride on morphine.

Originally introduced as a substitute for morphine, it has recently gained notoriety on account of its use by certain drug-takers. The hydrochloride of the alkaloid is the form in which it is most frequently employed, and, like the corresponding cocaine salt, it is usually taken as a snuff. Consequently, where this poison or cocaine is suspected, swabs should be taken from the mucous membrane of

the nose, and submitted to chemical examination. One sixth of a grain is stated to have produced fatal results, and one thirtieth of a grain has produced dangerous symptoms.

A fatal case of poisoning, described by W. R. Boyd in the *Medical Journal* of Australia, is quoted in the *Lancet* of May 3 of this year. In this case, 6.97 grains of heroine were administered in mistake for veronal, death ensuing seventy hours later, only  $\frac{1}{64}$  grain of morphine being found in the organs.

Heroine hydrochloride is a white crystalline substance with a bitter taste, easily soluble in water, and having a melting-point of  $230^{\circ}$  C., differing in this respect from morphine hydrochloride, which chars without melting.

It resembles morphine in its reactions with Frohde's solution, ferric chloride, and also with iodic acid and starch, but the colours produced are slightly slower in appearing. A 2 per cent. solution of hexamethylene tetramine in strong sulphuric acid gives a fine purple color very slowly turning blue; but in this instance also a very similar reaction is yielded by morphine and its salts. The sodium phospho-molybdate precipitate dissolves in ammonia to a blue color practically identical with that given by salts of morphine under similar conditions.

*Cocaine*,  $C_{17}H_{21}NO_4$ .—The hydrochloride, the usual form in which this alkaloid is found in commerce, occurs in white prismatic crystals, strikingly soluble in water (2 in 1) with a melting-point of  $186^{\circ}$  C.

It is employed medicinally as a local anesthetic in minor operations of the eye, throat, and mouth, but it has recently come into prominence from its illegitimate employment as a snuff. Its physiological effect appears at first to be stimulating, but this is sooner or later followed by lassitude and, in excessive doses, by a state of coma. It causes dilatation of the pupil and usually disturbances of the nervous system. The body soon becomes tolerant to the drug, and, in the case of habitual takers, little or none may be found in the organs after death. In this respect it would appear to resemble morphine (*cf.* Webster, *Analyst*, 1917, 42, 226).

In addition to its distinctive melting-point of  $98^{\circ}$  C., this alkaloid is characterized by the following reactions:

It possesses a bitter taste followed by a somewhat prolonged numbness of the tongue. When evaporated to dryness with a few

drops of nitric acid, and the residue moistened with a little alcoholic solution of caustic potash, it yields the characteristic odor of benzoic ether (meadowsweet).

Pisani (*Rend. Soc. Chem. Ital.*, 1914, 6, 132) states that with a 2 per cent. solution of hexamethylene tetramine in strong sulphuric acid a wine-red color is produced, becoming more intense as the temperature rises. I am unable to confirm this, as, under the conditions specified, no reaction is obtained beyond a slight charring produced by the rise of temperature.

The resorcinol and strong sulphuric acid test proposed originally by M. Goeldner (*Zeitsch, anal, Chem.*, 1901, 40, 820) is quite fallacious, as shown by L. A. Ryan (*J. Amer. Chem. Soc.*, 1915, 37, 1960), the lavender-blue color supposed to be indicative of cocaine being caused by traces of nitrous or nitric acid in the sulphuric acid employed.

Cocaine gives with a permanganate solution, under certain conditions, distinct and characteristic crystals, but special precautions are needed to get a satisfactory result. The modification of the test proposed by E. H. Hankin (*Analyst*, 1911, 36, 2), where the alkaloid is dissolved in a saturated alum solution and added to a dried film of potassium permanganate on a microscope slide, gives excellent results and the crystals are quite definite. The concentration of cocaine in the alum solution should not be less than 1 part in 10,000.

Although the salts of many alkaloids yield a precipitate with potassium chromate, cocaine hydrochloride gives no precipitate until after the addition of a few drops of concentrated hydrochloric acid. Morphine and heroine give no reaction with potassium chromate solution in either neutral or acid solution.

Wagner's solution (iodine in potassium iodide) throws down a brownish-red precipitate with salts of this alkaloid that appear as dark brown oily drops when examined microscopically. The same result was obtained with this reagent when cocaine hydrochloride was dissolved in saturated alum. Sodium phospho-molybdate gives a curdy yellowish-white precipitate soluble in ammonia to a very pale bluish-green solution.



ESTIMATION OF SMALL QUANTITIES OF LEAD IN  
FOOD AND SUBSTANCES CONTAINING  
CALCIUM PHOSPHATE.<sup>1</sup>

BY B. W. J. WARREN, F.I.C.

In the B.P. method for the estimation of lead, the substance to be tested is dissolved either in water or a dilute solution of ammonia.

With foods it is necessary to first destroy the organic matter and estimate the lead in the ash. The ash can be dissolved in dilute nitric acid, and the solution rendered alkaline with ammonia, a precipitate of calcium and magnesium phosphate being obtained. If the filtrate is used for the estimation of lead (using the B.P. method) considerable quantities of lead may sometimes be overlooked, as the lead is occluded with the precipitated phosphates (or as an insoluble double phosphate of calcium and lead).

Wilkie (*J. Soc. Chem. Ind.*, 1909, 28, 636) has pointed out that ferric hydroxide will remove lead from a tartrate solution.

If calcium phosphate containing traces of lead and copper is dissolved in dilute nitric acid and ammonia be added the precipitate contains all the lead, while the copper is in solution. If this precipitated phosphate (containing lead) is dissolved in dilute nitric acid the lead can be estimated colorimetrically.

In the absence of iron, lead and copper can be easily and accurately estimated in a food. Iron, however, presents some little difficulty: if a phosphate precipitate containing lead and iron (copper being eliminated as shown above) is dissolved in dilute acetic acid the solution is turbid owing to the presence of phosphate of iron. If this precipitate is filtered off some of the lead is removed with the precipitate (with the material with which I was working about two thirds were removed).

It is, however, possible to match the color with the slightly turbid solution and thus estimate the lead.

The method adopted is as follows:

Ten Grms. of foodstuff are incinerated in a silica dish, dissolved in a small quantity of water with the addition of 1 Cc. of nitric acid, filtered, and washed. To the filtrate, which should be colorless, a slight excess of ammonia is added, the precipitate filtered and

<sup>1</sup> Reprinted from *The Analyst*, June, 1919.

washed well. (The filtrate can be tested for lead by B.P. method.) The copper will be in the solution, while the lead (most, if not all) will be in the precipitate.

The precipitate is washed into a Nessler cylinder with water, 5 Cc. of dilute acetic acid are added, followed by an aqueous solution of hydrogen sulphide, and the color matched in the usual manner.

The control solution is prepared as follows:

A quantity of dilute lead solution (B.P.) diluted with water is rendered faintly alkaline with ammonia, and to this is added 5 Cc. dilute acetic acid and finally hydrogen sulphide solution.

The following results were obtained by the above method on samples prepared by adding lead to a food containing copper and iron:

Lead Added.	Lead Found.
10 parts per million.....	8, 9 parts
20 " " " .....	20, 16 "

SUTTON ROAD, SOUTHBEND.

## ESTIMATION OF MONOBROMATED CAMPHOR IN MIGRAINE TABLETS.<sup>1</sup>

BY W. O. EMERY.

### INTRODUCTION.

The estimation of monobromated camphor *per se* by means of its bromine content may be effected with greater or less facility by any one of several procedures, notably the classic one of Carius; more speedily, however, by that of Stepanoff<sup>2</sup> which involves reduction in absolute alcohol with sodium, or by modifications thereof as reported by Bacon,<sup>3</sup> Maryott,<sup>4</sup> and Drogin and Rosanoff.<sup>5</sup> The earliest recorded experiments dealing specifically with the quantitative elimination of the halogen in monobromated camphor were undertaken

<sup>1</sup> Reprinted from *The Journal of Industrial and Engineering Chemistry*, August, 1919.

<sup>2</sup> *Ber.*, 39 (1906), 4056.

<sup>3</sup> *J. Am. Chem. Soc.*, 31 (1909), 49.

<sup>4</sup> *Am. J. Sci.*, 30 (1910), 378; *Chem. News*, 103 (1911) 1.

<sup>5</sup> *J. Am. Chem. Soc.*, 38 (1916), 711.

by Schiff,<sup>6</sup> who, operating with sodium on a solution of the camphor derivative in toluene, showed the result of such action to be sodium bromide and sodium camphor. Taking advantage of this observation and subjecting the resulting products to titration *via* Volhard, Andre and Leulier<sup>7</sup> report satisfactory results in the examination of several commercial samples of the drug.

In medicaments like migraine tablets, however, the problem of evaluating the camphor derivative becomes more complicated. In addition to vehicular and other more or less inert materials peculiar to such products, we have here a preparation consisting essentially of acetanilide, caffeine, and monobromated camphor, with sometimes salicylates and plant extractives. From mixtures of this character monobromated camphor, on account of its physical properties, is hardly susceptible of quantitative isolation by means of immiscible solvents, although a gross separation of the drug in solution, along with acetanilide, caffeine, and other extractable material eventually present, may indeed be made by a systematic treatment of the powdered tablets with alcohol, benzene, or toluene. Such procedure, however, almost invariably gives rise to solutions of so unwieldy and varying a volume as to render any subsequent reduction, with sodium for example, quite valueless, owing to the uncertain quantity of metal required and consequent unsatisfactory results. Even when operating with like volumes of solvent, and in strict accord with the latest approved method comprehending the Stepanoff principle,<sup>8</sup> the amount of sodium required for complete reduction is generally variable and always relatively large, in fact, more than twenty times that of the bromine derivative involved. This comparatively low efficiency from the standpoint of sodium consumption arises from the phenomenon, familiar to most chemists, whereby metallic sodium when applied to heated alcohol immediately assumes the spheroidal state, moving about very actively on the surface of the liquid, but separated therefrom by a film or cushion of hydrogen and alcohol vapor, all conditions clearly favoring incomplete reduction. Any objection to, or uncertainty attendant upon, the use of the free metal may be entirely eliminated by recourse to the procedure whereby the powdered tablet itself in alcoholic solution and suspension is subjected to the action of sodium in the form of its mercury

<sup>6</sup> *Ber.*, 13 (1880), 1407.

<sup>7</sup> *J. pharm. chim.*, [7] 2 (1910), 64.

<sup>8</sup> *Loc. cit.*



amalgam, an effective reagent and at all times under complete control of the operator.

### EXPERIMENTAL.

The tabulated data are representative of numerous results obtained with both control and commercial mixtures. The monobromated camphor required for the controls was prepared by recrystallization of a well-known foreign brand carrying a slight excess of halogen. The purified product melted sharply at  $76^{\circ}$  and had a bromine content, as determined by Carius, of 34.6 per cent. In general, the treatment consisted in subjecting the powdered sample in alcoholic solution and suspension to the action of the amalgam at about the temperature of boiling alcohol, at first over a wire gauze and with appropriate reflux, finally on the steam bath to practical exhaustion of the amalgam, and with no attempt at condensation. The amalgam was applied in a strength of about 1 per cent. of sodium, although in Expts. 5 to 8, inclusive (see table), a product containing only 0.6 per cent. of sodium was employed. After quantitative separation of the liquid from the mercury, the halogen is precipitated by silver nitrate in acidified solution, and the insoluble bromide determined in the usual way. In general, estimation of the bromine *via* Volhard is not advocated, on account of possible interference from accompanying organic substances.

Experiment No.	$C_{10}H_{15}BrO$ Gram.	$PhNHAc$ Gram.	Caffeine Gram.	Starch Gram.	NaHg Gram.	AgBr Gram.	$C_{10}H_{15}BrO$ Calcd. G.	$C_{10}H_{15}BrO$ Calcd. Per Cent.
1	0.2000	....	....	....	25	0.1621	0.1994	99.7
2	0.1000	....	....	....	25	0.0810	0.0996	99.6
3	0.2000	....	....	....	25	0.1628	0.2002	100.1
4	0.1000	....	....	....	25	0.0809	0.0995	99.5
5	0.2000	....	....	....	25	0.1619	0.1991	99.6
6	0.2000	....	....	....	20	0.1617	0.1989	99.5
7	0.2000	....	....	....	15	0.1596	0.1963	98.2
8	0.2000	....	....	....	10	0.1526	0.1877	93.8
9	0.2000	....	....	....	15	6.1623	0.1996	99.8
10	0.2000	....	....	....	10	0.1622	0.1995	99.8
11	0.2000	0.8000	0.1000	0.1000	25	0.1627	0.2001	100.1
12	0.1000	0.4000	0.0500	0.0500	25	0.0812	0.0998	99.8
13	0.0972(?)	0.3888	0.0486	?	25	0.0762	0.0937	96.4(?)
14	0.0972(?)	0.3888	0.0486	?	25	0.0768	0.0945	97.2(?)
15	0.1000	0.4000	0.0500	0.2000	25	0.0812	0.0999	99.9
16	0.1296(?)	0.1944	0.0648	?	25	0.1052	0.1294	99.8(?)
17	0.1296(?)	0.1944	0.0648	?	25	0.1056	0.1299	100.2(?)
18	0.1300	0.2000	0.0650	0.1000	25	0.1059	0.1303	100.2
19	0.1296(?)	0.6480	....	?	25	0.1068	0.1314	101.3(?)
20	0.1296(?)	0.6480	....	?	25	0.1065	0.1310	101.1(?)
21	0.1300	0.6500	....	0.1000	25	6.1056	0.1299	99.9

In further explanation of these results, it may be stated that Expts. 1 to 10, inclusive, have to do primarily with the camphor derivative alone, 13 and 14, 16 and 17, and 19 and 20 with commercial mixtures, while 11 and 12, 15, 18, and 21 deal essentially with controls of the latter, in which the dominating ingredients were proportioned to agree with the manufacturer's label. Accordingly, any uncertainty existing relative to the quantities of such ingredients, notably monobromated camphor, actually introduced or present in the samples examined, would necessarily be reflected in all computations based thereon—as in the calculation of percentages—and is so indicated. With the exception of Expts. 3 and 4, the period of reduction in all the experiments was uniform, consisting of a  $\frac{1}{2}$  hr. treatment under reflux on the wire gauze and 1 hr. on the steam bath. In the exceptions noted, the reflux period was doubled, thus making the entire digestion cover a 2 instead of  $1\frac{1}{2}$  hrs. While no material advantage in the longer treatment is observable there can be no objection thereto. A brief survey of the results presented will suffice to show the efficacy of the method.

#### METHOD.

Ascertain the weight of 20 or more tablets, reduce to a fine powder and keep in a small tube or specimen bottle provided with a tightly fitting cork or glass stopper. On a metal or glass scoop weigh out an amount of the sample equivalent to not less than 100 or more than 200 Mg. of the camphor derivative alleged to be present. Transfer quantitatively with 20 Cc. of 96 per cent. alcohol and 10 Cc. of water, to a small (100 Cc.) round-bottomed flask, containing 15 G. of 1 per cent. sodium amalgam. Connect the flask, by means of a rubber stopper, with a short vertical reflux, preferably of the Allihn or of the worm type. Heat the mixture over a wire gauze just enough to cause the liquid to boil gently for a period of not less than 30 Min. After cooling slightly, wash out the condenser tube first with 5 Cc. of alcohol, then with 5 Cc. of water, receiving the washings in the flask below. Remove the flask to the steam bath, heating for another hour, or until the evolution of hydrogen has nearly or quite ceased. Toward the latter part of this operation, render the liquid about neutral with a few drops of acetic acid in order to further reduction. Transfer the contents of the flask to a separatory funnel, preferably of the Squibb type, withdrawing and

washing the mercury in a second separatory funnel with at least two 50 Cc. portions of water. Pass the several aqueous solutions quantitatively through a small filter, collecting the clear filtrate in a suitable beaker. Precipitate with silver nitrate after the addition of about 5 Cc. of nitric acid, and proceed in the usual gravimetric way, employing, if available, a Gooch crucible in the operation of filtering. The weight of the silver bromide multiplied by the factor 1.23 will give the quantity of monobromated camphor originally present in the sample taken for analysis. A control should be run on the amalgam in order to determine whether any correction is necessary for the presence of halogen in material quantity.

#### SUMMARY.

This method for the estimation of monobromated camphor in migraine tablets takes advantage of the fact that, when an aqueous-alcoholic solution of the camphor derivative, either alone or in admixture with other substances, is subjected to the action of sodium amalgam on heating, among other changes the bromine is split off quantitatively in the form of its sodium salt, which may then be determined gravimetrically in the usual way.

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#### ANTISCORBUTICS. II.<sup>1</sup>

In a previous issue of *THE JOURNAL*,<sup>2</sup> reference was made to some of the experiences which have led to the development of diverse sorts of antiscorbutic products available for the purposes of infant nutrition. It is not necessary to refer back to the older expeditions in search of the North Pole or to the experiences of our Civil War to learn how essential antiscorbutic foods may be to an adult as well as to the growing infant. The changes in our food supplies have altered the dietary habits of mankind,<sup>3</sup> and, although in normal peace times the tendency toward a liberal supply of varied

<sup>1</sup> From *The Jour. of Amer. Med. Asso.*, August 2, 1919.

<sup>2</sup> Antiscorbutics," I, editorial, *J. A. M. A.*, 73: 271 (July 26), 1919.

<sup>3</sup> Mendel, L. B., "Changes in the Food Supply and Their Relation to Nutrition," Yale University Press, 1916.



foods is likely to avert widespread deficiencies of essential factors, this is far from being the case under war-time conditions. Scurvy made its appearance in Europe among troops and civilians when the exigencies of the situation in which they were inadvertently placed compelled them to subsist on unsuitable foods. This does not necessarily mean that the energy furnished was insufficient, or that the protein was inadequate; but it has shown that even in the midst of plenty the quality of our foods may be dangerously defective.

The knowledge that heat may affect the stability of vitamins and more particularly the antiscorbutic property of foods has focused attention on the effects of cookery, canning and various other modes of food preparation and preservation on the integrity of the accessory food factors. We shall not claim the ability to render a final judgment as to either the safety or the nocuousness of any of the varied methods of conservation. A few references to the outstanding facts ought, however, to serve as an indication of the great uncertainties which have been raised, and the probable considerable significance of the questions at issue for practical dietetics. The keynote was sounded by Holst seven years ago. The striking demonstration of the loss of antiscorbutic potency as the result of desiccation and cooking furnished by Givens and Cohen<sup>4</sup> of Yale with regard to cabbage and potatoes has been substantiated at the Lister Institute in London.<sup>5</sup> We are told that, so far as animal experiments can be depended on to furnish evidence, there is a loss in antiscorbutic properties of more than 93 per cent. when cabbage is dried at a low temperature and stored subsequently from two to three weeks at laboratory temperature. After drying and storing from five to six weeks at laboratory temperature, a further loss of antiscorbutic properties is suffered. After storage for three months, nearly all the protective value of the fresh material is lost (about 96 or 97 per cent.). The fact that less loss through desiccation takes place if the product is first steamed or plunged into boiling water suggests at once that something other than mere heating or desicca-

<sup>4</sup> Givens, M. H., and Cohen, B., "The Antiscorbutic Property of Desiccated and Cooked Vegetables," *J. Biol. Chem.*, 36: 127 (Oct.), 1918.

<sup>5</sup> Delf, Ellen Marion, "The Antiscorbutic Value of Cabbage, I, The Antiscorbutic and Growth Promoting Properties of Raw and Heated Cabbage," *Biochem. J.*, 12: 416 (Dec.), 1918. Delf, Ellen Marion, and Skelton, Ruth Filby, "The Antiscorbutic Value of Cabbage, II, The Effects of Drying on the Antiscorbutic and Growth Producing Properties of Cabbage," *ibid.*, page 448.

tion is concerned in the deteriorating influences of these preservation processes.

From the standpoint of culinary food preparation, Delf<sup>5</sup> suggests that these facts have some bearing on methods of cooking green vegetables, and indicate broadly that the least loss of antiscorbutic properties will be obtained by cooking green vegetables for a short time at a higher temperature rather than for a longer time at a lower temperature. Hess and Unger<sup>6</sup> have lately reported that carrots lose much or all of their antiscorbutic potency through cooking. They have, furthermore, called attention to the added factor of the maturity of the plant. As they express it, from a nutritional standpoint carrots cannot be looked on as a uniform article of diet. There is a marked difference in various lots of carrots, and probably also of other vegetables, according to whether they are fresh and young, or are old. It was found, for example, that if, instead of employing the carrots which were ordinarily fed to their laboratory animals, they gave the same amount of fresh young carrots, plucked only a few days previously and cooked, not only did the animals not develop scurvy, but they gained steadily in weight for a long period.

Hess and Unger<sup>6</sup> remark that the freshness and age of the vegetables sufficed also to enable them to retain their antiscorbutic potency after dehydration. This is a statement of considerable importance because it points to a further variable that may need to be considered in evaluating food preparations from the standpoint of their antiscorbutic effects. If, to the problem of the effect of heat, oxidation, preliminary treatment and age of the fresh product, there is added the question as to the possible influence of different reactions of acid and alkali as they occur naturally in foods or are added incidental to their manipulation—the complexity of the project of retaining the antiscorbutic potency becomes more apparent.

This is a time for cultivating the "open mind" in reference to the true nutritive value of conserved foods. If some desiccated vegetables have proved to be devoid of antiscorbutic efficiency, it must, nevertheless, be admitted that the loss can probably be averted entirely or partially when the conditions which determine it are definitely ascertained. Fruit juices have already been concentrated, and tomatoes have already been dehydrated without becoming im-

<sup>6</sup> Hess, A. F., and Unger, L. J., "The Scurvy of Guinea-Pigs, III, The Effect of Age, Heat and Reaction on Antiscorbutic Foods," *J. Biol. Chem.*, 38: 293 (June), 1919.

potent in respect to the factor under discussion. Hess and Unger assure us that it would be an error to infer from such experiments as are now on record that milk necessarily loses its antiscorbutic potency when it is reduced to a dry state. Enough specific instances of contradictory facts are on record to warn us, on the one hand, against condemning canned goods or dehydrated vegetables of their analogues from the standpoint of their vitamin potency; or of praising any of them without specific information as to each product. The offhand statements which are beginning to emanate from partisan or inadequately informed sources must not be accepted. The time is not yet ripe for "expert opinions" that are all comprehensive in their information. Knowledge in relation to vitamins is in the making. Fortunately, at the point where chemical analysis utterly fails, the physiologic experiment is proving to be a dependable guide. Let us get the facts first of all.

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## PHARMACY IN THE BELGIAN ARMY.<sup>1</sup>

The medical service of the Belgian Army is very far from being a concrete body of officers and men—like our Royal Army Medical Corps—charged with doing anything and everything for the wounded or sick soldier anywhere or at any time. The *Corps de Santé Militaire* includes medical officers, pharmacists, and veterinary officers. The Medical Service consists of the medical and pharmaceutical officers of this corps plus the hospital section of the *Bataillon d'Administration*.

### RANK AND TITLES.

In the Belgian Army the position of doctors and pharmacists is very similar to the status they hold in the French Army. Neither medical nor pharmaceutical officers have military titles, and, in consequence, they have not the standing in their Army which long experience has proved in our own and other armies can alone be secured by a military title. The following are the titles held by medical officers in Belgium:

*Médecin Inspecteur-General*, ranking with major-general.  
*Médecin Principal de Ire Classe*, ranking with colonel.

<sup>1</sup> From *The Chemist and Druggist*, August 30, 1919.



*Médecin Principal de 2me Classe*, ranking with lieut.-colonel.

*Médecin de regiment de 1re Classe*, ranking with major.

*Médecin de regiment de 2me Classe*, ranking with captain.

*Médecin de bataillon de 1re Classe*, ranking with lieutenant.

*Médecin Adjoint de 1re Classe* and *Médecin Adjoint de 2me Classe*, both ranking with second-lieutenant.

Readers of my article on "Pharmacy in the French Army" (*C. and D.*, June 7, p. 50) will note that the historic title of the French *Médecin*, viz., "major," is not used in Belgium. The rank of "major" does not exist in the French Army. The corresponding rank is, of course, *Commandant*; but the term *Monsieur le Major* is universally employed by the French *poilu* in addressing his medical officer. The title is obviously a contraction of the cumbrous French medico-military titles of *Médecin Major* and *Médecin Aide Major*, but takes some getting used to in one's earlier days with a French military formation. During the war it was sometimes replaced by a word of *argot* (*Tout-bib*), as the chief amusement of the *poilus* in the trenches was to invent new words and phrases of *argot*.

#### RANKS AND TITLES OF PHARMACISTS.

There are seven grades of pharmacist in the Belgian Army, viz.: *Pharmacien en Chef*, ranking with lieutenant-colonel.

*Pharmacien Principal*, ranking as major.

*Deuxième Pharmacien de 1re et 2me Classe*, both ranking as captain.

*Pharmacien de 3me Classe*, ranking as lieutenant.

*Pharmacien de 4me Classe* and *Pharmacien Adjoint*, both ranking as second lieutenant.

The proportion of pharmacist to medical officers is about one to four.

#### PAY.

The rates of pay drawn by pharmacist officers is, as in the Italian Army (*C. and D.*, June 14, p. 64), the pay of their relative rank, as all branches of the service are paid at the same rates. A *Pharmacien en Chef* draws only 280 l. per annum, a *Pharmacien Principal* 252 l., *Pharmacien de 1re et 2me Classe* from 168 l. to 204 l., *Pharmacien de 3me Classe* 130 l. It will be seen that some pharmacists, with merely non-commissioned rank, in our Army are better off financially than their commissioned Belgian *confrères*.

## RECRUITMENT OF THE MEDICAL SERVICE.

There is nothing corresponding to the Royal Army Medical College or the *Val de Grâce* in Belgium, and our R. A. M. C. is replaced by a portion of what is called the *Bataillon d'Administration*. This administration includes all the administrative service, and three sections of it are known collectively as *Le Service de Secours de l'Armée*. One of these sections is the *Section des Hopitaux*, and the other two correspond to our Royal Army Veterinary Corps and the Royal Chaplains Department. The *Section des Hopitaux* is divided into *personnel d'ordre* or permanent administrative officials and *personnel technique* or executive personnel, which may be what we would call "regular" or on the reserve. A student of pharmacy or a qualified *Pharmacien* enters the Medical Service by enlisting in the *Section des Hopitaux*, in which he is graded according to his professional standing. Junior students of pharmacy are graded as *Pharmaciens Aspirants*, and senior students and graduates in pharmacy as *Pharmaciens Auxiliaires*. Both wear the uniform of a *Pharmacien Adjoint*, but without embroidery, lace, or stars. They go through a course of instruction, under a regular pharmaceutical officer, but receive no pay unless they are mobilized or specially employed. *Pharmaciens Auxiliaires* who wish to obtain commissions as *Pharmaciens Adjoints* must pass a special examination when they are graded as *Pharmaciens Suppléants*. Vacancies in the rank of *Pharmacien Adjoint* are filled up from among the *Pharmaciens Suppléants*, who must have graduated in pharmacy at one of the universities. Instead of proceeding to a permanent commission in the Army, a *Pharmacien Suppléant* may pass to the reserve by applying for *congé illimité*, or permanent leave. The bulk of the leading pharmacists of Belgium were, before the war, *Pharmaciens Suppléants* on permanent leave.

## PHARMACEUTICAL RANK AND FILE.

The pharmacy and laboratory attendants of the service are also recruited from the *Bataillon d'Administration*. Together with the nursing orderlies, they form a small part of the staff of a Belgian military hospital, as the bulk of the administrative work is in the hands of non-medical officers. The management of the hospital is quite distinct from the actual care and treatment of the sick. Not even the medical records of the formation are kept by medical per-

sonnel. The medical officer in charge demands such clothing, bedding, and diets as he may require, and what corresponds to a Royal Army Service Corps officer, or subordinate, furnishes him with his requirements and looks after the furnishing, lighting and cleanliness of every part of the hospital except the actual wards. This system of dual control is in sharp contrast to the arrangements of our own Army, where the R. A. M. C. officer in command is responsible for every detail of its organization, and where practically all the work of the unit is carried out by medical *personnel*. In order to understand how the pharmacist officer fits into the Belgian fighting machine it is necessary, as in the case of the French and Italian armies, briefly to glance at the field medical organization of the Army. The organization corresponds very closely to that of the French, but the formations have different names. It comprises the following:

1. The Regimental Medical Service.
2. *Les Colonnes d'Ambulance*, corresponding to the French Army.
3. *Les Hopitaux Volants*, corresponding to the French ambulances.

Later in the war the official title was dropped, and the term *ambulance* adopted. The Regimental Medical Service is organized on French lines, and each regiment has a little medical hierarchy of its own, directly under the *Colonel du régiment*, as in the French system, but there was a tendency to attach *Pharmaciens* to regiments, as a feature of the Belgian Service is the establishment of *Infirmaries du régiment* for the treatment of trivial cases. One point about all these little regimental hospitals was, throughout the war, a well-equipped and well-organized pharmacy. The *Colonne d'Ambulance* functions exactly like the French *Groupes des Brancardiers Divisionnaires* or the Bearer-Division of a British Field Ambulance. There is a *Pharmacien* and a *Pharmacien Adjoint* with each unit and, in addition to pharmaceutical duties, the pharmacist officers function as analysts and gas officers in the same manner as their *confrères* in the French *Service de Santé*.

#### THE FIELD HOSPITALS.

The *Hopitaux Volants* in the Belgian Army have each got a *Pharmacien* officer, and usually two *Pharmaciens Suppléants*. As



already pointed out, these formations are identical with the French Ambulances and, as in the French Army, there are two with each division.

For the pharmaceutical administration in the field, the Director of Medical Services of a Belgian Army has one *Pharmacien Principal* and one *Pharmacien Suppléant* on his staff. The *Pharmacien Principal* of the Army is responsible to the director for the organization of pharmaceutical services, laboratories, and medical stores throughout the Army area. He carries out inspections on the part of his chief and functions in every way as a senior staff officer at the Army headquarters. The *Pharmacien Suppléant* acts as staff officer to his chief and carries on the duties of the pharmaceutical section of the director's office during the absence on duty of the *Pharmacien Principal*. All base and advanced depots of medical stores are in the charge of *Pharmaciens*. Indeed the British Army is the only European Army in which the care of medical and surgical material is not in the hands of trained pharmacist officers.

#### THE RED CROSS.

As in most other Continental countries, the Red Cross Society of Belgium is very highly organized, and employs a large number of pharmacists. The society is under a Committee of Direction, appointed by the King, and works in conjunction with the Belgian War Office. Under certain conditions, laid down by the military authorities, a pharmacist can complete the bulk of his military service under the Red Cross. The peace activities of the Belgian Red Cross were not at all comparable with those of other Allied Red Cross Societies such as the *Croce Rossa Italiana*. The society provides the personnel for ambulance trains and railway rest stations, and organizes auxiliary military hospitals of various kinds.

It will be seen that the pharmaceutical service of the little Belgian Army presents some interesting characteristics; that pharmacy holds the status of a profession and its practitioners who are granted commissioned rank hold responsible posts as officers on the staff. (*M. D., L. P. S. I.*, 87, 1919.)

## AN EXPERIMENTAL STUDY OF STROPHANTHUS KOMBÉ SEEDS.<sup>1</sup>

BY KARAM SAMAAAN, M.Sc.

### PART I.

This experimental study of *Strophanthus Kombé* seeds was carried out with the object of finding out (*a*) The activity or otherwise of the oil present in the seeds; and (*b*) the existence or non-existence in the de-fatted seeds of a physiologically active body beside the water-soluble strophanthin.

A special feature of this investigation is the pains which were taken to ensure absolute purity and freedom from water of the solvents used and the thorough drying of the seeds. The various solvents used—petroleum ether, ether, ethyl alcohol, methyl alcohol, amyl alcohol, and chloroform—were subjected, in the laboratory, to lengthy purification processes and thorough drying.

The seeds were dried in an oven—fitted with a thermostat and the temperature adjusted at 40–50° C.—for four successive days of eight hours each. The total loss of weight reckoned as moisture was 6.85 per cent. of the original seeds.

The dried seeds were de-fatted by means of purified and dried petroleum ether b.p. 50–70° C. The amount of oil isolated was 31.55 per cent. of the original seeds. This oil was found to possess no marked physiological action. This was established by (*a*) injecting and feeding frogs with a preparation of the oil, or the oil itself; and (*b*) perfusing a weak emulsion of the oil through the frog's heart. Great care was also taken to ensure uniformity of conditions in the physiological experiments carried out.

It was noticed that on shaking the oil with water and leaving it for a time a yellowish white solid body—probably resinous in nature—separated from the oil. The layer of oil became less viscid and more transparent than the original sample. The isolated resin-like body was found to be soluble in ether, petroleum ether, alcohol, and chloroform. It was precipitated from alcoholic and ethereal solutions by excess of water containing 1 per cent. hydrochloric acid.

Since the oil before separation of this resin-like body was found to be inactive, no attempt was made to examine the latter.

<sup>1</sup> Reprinted from *The Pharmaceutical Journal and Pharmacist*, July 26, 1919.

## SUMMARY OF RESULTS.

No. of Experiment.	Weight of De-fatted <i>Strophanthus</i> Seeds Exhausted	Volume of Solvent Used.	Period of Exhaustion (16 Hours' Maceration and 8 Hours' Continuous Exhaustion a Day).	Taste of the Seeds After Exhaustion.	Weight of Dry Residue Obtained After Evaporation of the Solvent.	Chemical Tests made on the Residue.	Residue Tested Physiologically.
1	30 gms.	800 cc. water.	6 days.	Tasteless.	6.87 gms.	Positive.	Active.*
2	30 gms.	800 cc. absolute alcohol.	13 days.	Bitter.	3.75 gms.	Positive.	Active.*
3	30 gms.	800 cc. amyl alcohol.	13 days.	Bitter.	3.85 gms.	Positive.	Active.*
4	30 gms.	800 cc. methyl alcohol.	10 days.	Tasteless.	5.95 gms.	Positive.	Active.*
5	30 gms.	800 cc. chloroform.	13 days.	Very bitter.	2.84 gms.	Faintly positive	Slightly active.*

\* The physiological action of these residues was practically identical within limits. In brief, it consisted in slowing the heart, prolonging the period of systole, and in being non-cumulative. This was established by perfusing solutions of these residues through the exposed heart of a pithed frog and tracing the heart beats on smoked paper on a revolving drum.

The seeds that were exhausted with water, exp. I, were dried and then exhausted with absolute alcohol. The residue obtained after evaporation of the absolute alcohol was found to be inactive, thus showing that absolute alcohol does not remove any physiologically active body from the seeds which were previously exhausted with water.

The aqueous residue obtained as in exp. I was exhausted with amyl alcohol. The amyl alcohol removed the bitter principle and left a tasteless residue which was found to be physiologically inactive. The chemical tests made on this residue were negative.

The absolute alcohol residue obtained as in exp. II, the amyl alcohol residue obtained as in exp. III, the methyl alcohol residue obtained as in exp. IV, the chloroform residue obtained as in exp. V, were each exhausted with water. The water removed all the bitter principle and left a tasteless residue which in each case was found to be physiologically inactive, and whose chemical tests were negative.



The seeds de-fatted with petroleum ether were then exhausted with ether, yielding 0.415 per cent. residue, which was found to be physiologically inactive.

One may conclude, therefore, that the activity of the oil and the ether extract obtained by some previous investigators was probably due to the seeds and solvents not having been well dried.

The de-fatted seeds, obtained as above by treatment with petroleum ether and ether, were exhausted with various solvents, and the activity of the residue left after evaporation of the solvent determined physiologically and chemically in each case.

Exhaustion was carried out by means of a Soxhlet apparatus and under reduced pressure, so that the temperature did not exceed 60° C., so as not to cause decomposition of a physiologically active body. This was more necessary as the seeds were not readily exhausted of their bitter principle—even water (the best solvent) requiring a period of six days, during which two processes alternated—(a) continuous exhaustion for eight hours, followed by (b) sixteen hours of simple maceration.

In brief the above work may elucidate the following points:

1. The oil of *Strophanthus Kombé* seeds isolated by dry petroleum ether is inactive.
2. The ethereal residue is inactive.
3. The poisonous property of the seeds is due to a water-soluble glucoside or glucosides.
4. No active principle other than the water-soluble body was removed by any of the solvents employed.
5. Water completely removes the active principle from the seeds.
6. Methyl alcohol comes next to water in being a good solvent for the active principle.
7. Neither absolute alcohol nor amyl alcohol did completely remove the bitter principle from the seeds—probably due to the coagulation of the proteid substances, and thus prevent thorough contact of solvent and solute.
8. Amyl alcohol completely removes the bitter principle from the aqueous residue but not from the seeds.
9. Chloroform is a very poor solvent for the active principle.
10. The water-soluble glucoside or glucosides slow the heart, prolong the period of systole, and are non-cumulative.

The chemical tests utilized in the above table are: (1) The sulphuric acid (80 per cent.) test; (2) the ferric chloride and sulphuric

acid test; (3) the sulphuric acid and potassium dichromate test; (4) the phosphomolybdic acid test; (5) Keller-Kiliani's test; (6) Kiliani's reagent; (7) Keller's test; (8) the tannic acid test; and (9) a new delicate test which is as follows: Sulphuric acid concentrated (2 drops) and ammonium molybdate (0.10 Gm.) on a slab gave with a trace of strophanthin—or residue containing strophanthin—a light brownish green color which gradually developed into blue after ten minutes. The intensity of the blue color reached a maximum in twenty minutes, and remained permanent. This intense blue color was instantaneously destroyed by a trace of concentrated nitric acid. This test is based on the reducing power of the glucose portion of the strophanthin molecule, and, therefore, this test would be positive with other active principles of a reducing nature.

This test may be used as a comparative test for different varieties of strophanthus seeds.

Several active principles, particularly the glucosides, were tested with this test.

Some of these results may be interesting in connection with strophanthin:

Digitalin (verum)—Garnet red at once, going to deep blue in a minute.

Digitalein (Merck)—Orange at once, going to orange red in two minutes, then deep blue in twenty minutes.

Digitoxin (Merck)—Olive green at once, going to dirty black in a minute, then changing to deep blue.

Digitalin pur. (Merck)—Orange at once, going to violet in half a minute, and gradually to blue in five minutes.

Digitonin (Schuchardt)—Nothing at first; blue color appears in two minutes, reaching a maximum in eight minutes.

Salicin—Violet immediately, going to blue in eight minutes.

Santonin—Light blue, deepening on keeping.

## PART. II.

The determination of the M.L.D. of

(I) K. Strophanthin isolated in the laboratory.

(II) Strophanthin Merck, and

(III) Tincture of Strophanthus B.P., 1914.

English frogs were chosen for these experiments, and the usual

methods of M.L.D. determinations were adopted. The following are the final conclusions drawn from 59 experiments:

M.L.D. by intralymphatic injection for each kilogram of body weight of frog:

0.00104 Gm. of K. Strophanthin isolated in the laboratory.

0.00107 Gm. of Strophanthin Merck.

1 Cc. of Tincture of Strophanthin B.P.

Oral M.L.D. for each kilogram of body weight of frog:

0.02 Gm. of K. Strophanthin isolated in the laboratory.

0.0208 Gm. of Strophanthin Merck.

20.40 Cc. of Tincture of Strophanthus B.P.

From these results one may conclude that:

(1) For a frog the oral M.L.D. is about twenty times more than the M.L.D. given by intralymphatic injection.

(2) The toxicity of K. Strophanthin (isolated in the laboratory) is practically identical with that of Strophanthin Merck.

### PART III.

The same B.P. Tincture of Strophanthus whose M.L.D. was determined in Part II. was assayed by the following methods and gave the following results:

- (i) 0.082 per cent. of Strophanthin in the tincture as assayed by Elborne's method ("Year-Book of Pharmacy," 1887, 423).
- (ii) 0.086 per cent. of Strophanthin in the tincture as assayed by Fraser's method (*P.J.*, 1889, 332).
- (iii) 0.097 per cent. of Strophanthin in the tincture as assayed by Barclay's method (*P.J.*, Nov. 28, 1896, 463).
- (iv) 0.102 per cent. of Strophanthin in the tincture as assayed by Fromme's 1910 method (*E. Ph.*, vol. II., 1915, p. 129).
- (v) 0.101 per cent. of Strophanthin in the tincture as assayed by Lampart and Mueller's method (*A. Pharm.*, ccli., 609).
- (vi) 0.104 per cent. of Strophanthin in the tincture physiologically assayed.

The above results show that Barclay's, Fromme's 1910, and Lampart and Mueller's methods agree—within limits—with the physiological standardization and are, therefore, satisfactory.

It was noted that it would be preferable to use a perforator—instead of shaking out in a separating funnel—in removing the strophanthidin by chloroform, as this would minimize the amount of



chloroform used and assure complete removal of the strophanthidin. The same B.P. tincture assayed by Barclay's method and using the perforator gave 0.099 per cent. of strophanthin.

In assaying the seeds by Fromme's and Lampart and Mueller's methods, I was unable to remove completely the bitter principle by the methods they used, which consist in exhausting the seeds with absolute alcohol. It is probable that the samples of seeds they investigated were not as rich in the glucoside as the sample I investigated. In the assay of the seeds, I found it better that the extraction should be done, not by absolute alcohol, but by 65 per cent. alcohol in a long narrow percolator till the seeds were free from bitterness.

Working under the same conditions, I tried a series of experiments for exhausting the de-fatted seeds and examining both the tincture and the marc obtained, and arrived at the following conclusions:

1. Absolute alcohol is not a good solvent for the active principle present in the seeds.

2. The lower the percentage of alcohol, the more rapid is the removal of the active principle from the seeds.

3. A lower percentage of alcohol than 65 per cent., though it extracts the bitter principle more rapidly, yet it produces an unsightly tincture, which is not clear, and is very hard to filter.

4. Water alone is unsuitable, since the aqueous tincture decomposes very quickly; a precipitate was formed, and a bad odor developed within two days.

5. The best method to prepare a tincture, on the large scale, is to moisten the de-fatted seeds with alcohol 65 per cent. Then employ slow extraction (by 65 per cent. alcohol) in a long narrow percolator till the seeds are free from bitterness. A sample of the resulting tincture should be assayed both chemically and physiologically, and then the tincture diluted with 65 per cent. alcohol to an official strength.

This method of procedure is suggested since different samples of seeds—and hence the tinctures prepared from them—vary to a considerable extent in the strophanthin content.

These investigations were carried out in the pharmacological laboratories of the Manchester University, and I take this opportunity to express my best thanks to Professor R. B. Wild, M.D., M.Sc., F.R.C.P., and Mr. J. Grier, M.Sc., Ph.C., for their valuable suggestions and criticism.

## TRITICUM REPENS: A COMMERCIAL RARITY.<sup>1</sup>

BY JAMES SMALL, D.Sc., Ph.C., F.L.S.

Some time ago Mr. E. M. Holmes informed me that there was a scarcity of genuine couch grass in commerce, and suggested that a microscopic investigation of the material being sold as *Triticum repens* would be of interest, the principal point being the identification of the botanical source of the commercial product. At his request I examined properly authenticated material of various species of grasses, and also a number of commercial samples. The result of this investigation is summarized in the title. *Triticum repens* is a commercial rarity, and the chief, if not the only, substitute is the rhizome of *Cynodon Dactylon*, the dog grass.

The method of examination was simple. Transverse sections of pieces from each authentic sample were prepared and double-stained with methylene blue and erythrosin. Similar unstained sections were prepared from the commercial samples, and a comparison was made. The rhizomes all have the usual scattered vascular bundles, with a few large vessels. They also agree in having a certain amount of sclerenchyma, and it is particularly by the amount and distribution of this tissue that the different species can be identified.

### DESCRIPTION.

*Triticum repens*.—There are two rings of sclerenchyma, an outer ring, three or four cells wide, forming a hypodermis and a broader ring forming a common sheath to the vascular bundles, and at the same time completely enclosing the outer bundles (Fig. 1). A few small bundles occur in the cortex surrounded by a single row of sclerenchymatous cells. In mature rhizomes the pith shows some disintegration, and the center of the section is hollow.

*Cynodon Dactylon*.—Only one ring of sclerenchyma is present, forming a wavy band inside the narrow cortex and around the outer part of the rhizome. The cortex in this case is narrower than in *Triticum repens*, and it encloses no small vascular bundles. The scattered bundles within the ring of sclerenchyma have each a bundle sheath of the same tissue one or two cells wide. Dog grass rhizome

<sup>1</sup> Reprinted from *The Pharmaceutical Journal and Pharmacist*, July 26, 1919.

is usually oval in section, and at each end of the oval two lacunæ occur in the cortex. Within the sclerenchyma a large number of scattered vascular bundles occur. The most distinctive feature of this rhizome, however, is that all the cells of the ground tissue within

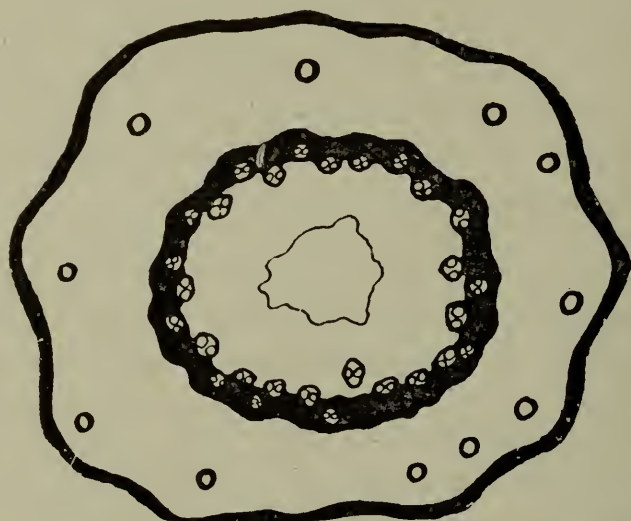


FIG. 1. *Triticum repens.*

the sclerenchyma have comparatively thick walls and are *filled with starch grains* (Fig. 2). Starch does not occur in any quantity in any of the other species examined. This starch gives a character-



FIG. 2. *Cynodon Dactylon.*

istic white appearance to the cut surface of the rhizome. The center is frequently, but not always, hollow as in couch grass.

Commercial samples can be examined for this grass very easily. A clean, transverse cut with a sharp knife or a razor displays the



two lacunæ and the yellowish ring of sclerenchyma. A drop of tincture of iodine gives a black color with the white, starchy surface.

*Holcus mollis*.—The ring of sclerenchyma in this case is more or less hypodermal, like the outer ring in *Triticum repens*. It is at least twice as broad, and encloses some vascular bundles. Small islands of parenchyma occur at intervals below the epidermis, and rudimentary stomata are present outside such groups of cells (Fig. 3). Each of the scattered, central, vascular bundles has a

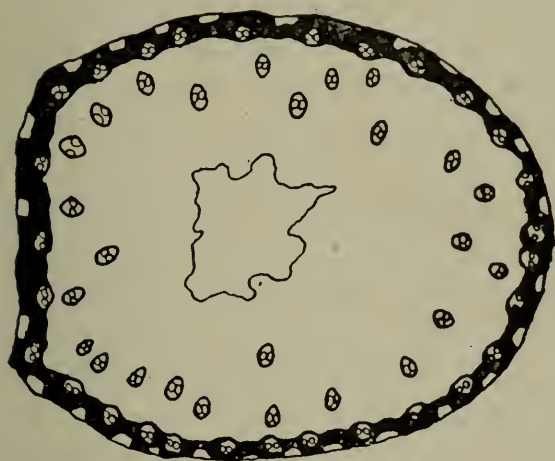


FIG. 3. *Holcus mollis*.

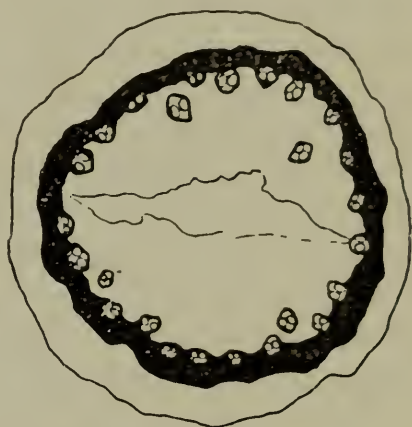


FIG. 4. *Agrostis vulgaris*.

sclerenchymatous sheath one or two cells wide. This species resembles dog grass in the oval shape of its section and in the hollow center, but it can readily be distinguished by the absence of starch and by the absence of any ring of ground tissue outside the sclerenchyma. Inosite or some other nutritive substance occurs in the outer part of the rhizome in the form of small, white grains, which do not stain blue with iodine. The cortex is three or four cells wide, as in *Cynodon*, and contains no small vascular bundles.

*Agrostis vulgaris*.—The ring of sclerenchyma forms a common sheath to the vascular bundles, like the inner ring of *Triticum repens*. This ring completely encloses the outer scattered bundles, and other bundles occur inside the ring, each with a sclerenchymatous sheath, one or two cells wide. The section may show no hollow center, or some disintegration may be present, giving a crack (Fig. 4) or a hollow center.

## EXAMINATION OF SAMPLES.

No. 1 was part of an ordinary commercial sample in the Museum of the Pharmaceutical Society, and was found to consist of pure *Triticum repens*.

No. 2 was another museum specimen from the School of Pharmacy collection, and was genuine *Triticum repens*.

No. 3 was collected at a Kentish farm, and was genuine *Triticum repens*.

No. 4 was the only recent commercial sample which consisted entirely of *Triticum repens*. It is described as couch grass, "Glad."

No. 5 was a commercial sample obtained from a wholesale firm, and consisted of 75 per cent. *Triticum repens* with 25 per cent. *Cynodon Dactylon*.

No. 6 was dog grass, sold as couch grass, by a foreign herbalist. It was pure *Cynodon Dactylon*.

No. 7 was another sample of dog grass, and consisted entirely of *Cynodon Dactylon*.

Nos. 8, 9, 10, 11, 12, and 13 were samples from four wholesale firms, and were all pure *Cynodon Dactylon*.

No. 14 was a sample from one of the same firms, and contained a few fragments of an unidentified grass rhizome with no sclerenchyma, and with the cells full of starch. The great bulk of the sample was again *Cynodon Dactylon*.

No. 15, an old retail sample, was *Triticum repens*.

## DISCUSSION.

*Triticum repens*, or couch grass, is a common but rather variable grass occurring throughout Britain in cultivated ground and waste places, by the roadsides and on the seashore. It is regarded as a weed in pasture and arable land. It is dragged out of the fields and left at the edge for burning by the farmer or for collection by the herbalist.

*Cynodon Dactylon*, or dog grass, is very rare in Britain, occurring only on the South Coast of England. It is very common on the sea coast in the South of France and in Spain. It is regarded as the best pasture grass in India, where it is very abundant.

These were both known in commerce. It seemed possible, however, that some common British grass was being used, and *Holcus mollis*, or soft grass, a fairly common grass in woods and pastures

and by hedges, and *Agrostis vulgaris*, or bent grass, a very common grass on dry heaths and pastures and by roadsides were therefore examined. Neither of these grasses is a fodder plant. The former is a weed which is treated like couch grass by the farmer, and the latter is said to be disliked by cattle. Neither of these species was present in any of the samples.

The therapeutic value of *Triticum repens* is somewhat obscure, and the question arises whether *Cynodon Dactylon* may not have the same or a similar action. The solution of that problem is outside the scope of this investigation, which is a purely botanical inquiry into the source of the present supply of commercial couch grass. The botanical source is undoubtedly *Cynodon Dactylon*, and the history of the trade in drugs during the war suggests that Spain is the geographical source of the material. Zufall, in a recent article on couch grass, in the *Journal of American Pharmaceutical Association*, has also identified *Cynodon Dactylon* as the chief adulterant of and substitute for the U.S.P. *Triticum*.

Acknowledgments are due to Mr. E. M. Holmes for bringing the problem to my notice and for supplying a number of specimens; also to Professor H. G. Greenish for some of the samples.

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## SODIUM MORRHUATE IN TUBERCULOSIS.<sup>1</sup>

Reference was made last year (*Prescriber*, 1918, p. 149) to the introduction of a sodium salt of the fatty acids of cod-liver oil, known as sodium morrhuate, as a remedy for tuberculosis. Sir Leonard Rogers was led to think of this preparation by the success of intravenous injections of sodium gynocardate in leprosy. He now (*Brit. Med. Jour.*, 1919, I, 147: Feb. 8) gives a full report of the new product.

Sodium morrhuate is made from the unsaturated fatty acids of cod-liver oil after extraction by ether, by a process similar to that by which sodium gynocardate (see *Prescriber*, 1918, p. 123) is made from chaulmoogra oil. A 3 per cent. aqueous solution, sterilized, with the addition of 0.5 per cent. phenol, may be injected subcutaneously, with very little pain, and also intravenously. A year's experience has shown that such injections are of great value in leprosy, which proves that there is nothing specific in chaulmoogra oil, and

<sup>1</sup> Reprinted from *The Prescriber*, July, 1919..



supports Roger's view that these salts act in some way on the coating of the acid-fast bacilli. He is satisfied that sodium morrhuate is harmless.

The usual initial dose is 0.5 Cc. of the 3 per cent. solution, increased by 2 to 4 minims at each injection, which may be given two or three times a week until any reaction occurs; then a week's interval is left, and the dose reduced. Injections are given subcutaneously until they reach an inconvenient size, such as 2 Cc., when intravenous injections can be begun with 0.5 Cc. gradually increased in the same way.

Clinical trials of sodium morrhuate in phthisical cases have been made by E. Muir and others, and the results are distinctly encouraging. Rogers, in summing up these results, says that he is convinced of its harmlessness, which is more than can be said of tuberculin. "At the same time," he adds, "the fact that sodium morrhuate causes febrile and local reactions necessitates great caution in pushing the drug beyond the limits which have so far proved safe, and a warning is required regarding the possibility of harm being done by its injudicious use. With this caution I feel that the results already obtained justify me in bringing sodium morrhuate to the notice of the medical profession, to allow of the prolonged trials by many skilled workers, which will be necessary before its permanent value, if any, can be decided, and the indications and contraindications for its use worked out."

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#### WESTERN AUSTRALIAN SANDALWOOD OIL.<sup>1</sup>

The January-March, 1919, issue of the *Bulletin of the Imperial Institute* contains an interesting article on the sandalwood of Western Australia, by Mr. C. E. Lane-Poole, conservator of forests in Western Australia, in which he criticizes a previous note in the *Bulletin* (January-March, vol. XV., No. 1) dealing with the production of sandalwood oil in Mysore, and in which reference is made to western Australian sandalwood, which Mr. Lane-Poole asserts hardly does justice to that product. The *Bulletin* stated that "so-called sandalwood exported from Australia" is mainly derived from *Fusanus spicatus*, but Mr. Lane-Poole cites botanical authorities such as Baron von Mueller, Dr. F. L. Stoward, and De Candolle,

<sup>1</sup> Reprinted from *The Chemist and Druggist*, September 6, 1919.

showing that the genus *Fusanus* approaches so closely the genus *Santalum* that, if finely drawn distinctions are waived, it may be regarded as identical with it and is merely a synonym as the Kew Index shows. Mr. Lane-Poole mentions that the western Australian sandalwood tree yields a sandalwood oil which is practically identical, chemically and pharmacologically, with that obtained from sandalwood from other sources of supply. Continuing he says that: "Discussion as to verbal differences in botanical classification of western Australian sandalwood reaches satisfactory finality when the oil obtained from the trees comes under notice. Many years ago, when sandalwood was fairly plentiful in those areas of western Australia now occupied almost exclusively by agriculturists, sandalwood oil was manufactured; but for various reasons the trade was never developed. Of recent years a start has again been made, and an oil produced which has found a ready sale. The santalol content of the western Australian oil varies from 75 to 80 per cent., but the oil has not yet been officially recognized by the British and American Pharmacopœias because there has hitherto been present in it a certain small percentage of sesquiterpene ethyl. Therapeutically, the presence of this foreign element has formed no bar to its success. The oil has been, and is, used in the Public Hospital at Perth and in other hospitals in Australia, and there is evidence that the sesquiterpene ethyl is as actively curative as the santalol in the oil. But its presence was held to place the oil below the standard demanded by the Pharmacopœias. The manufacturer here, having found ready sale for his product at fair prices, did not at the outset attach much importance to the foreign element in his oil. But the increased demand arising through the war induced him to make efforts to bring his product up to British Pharmacopœia requirements. With this view he submitted it to a chemist of repute in London, and has, within the last few months, learned that a process has been found which entirely eliminates the sesquiterpene ethyl, thus at once placing the western Australian product on a par with Mysore oil and meeting the B. P. standard. The figures given in the *Bulletin* note as to the value of the sandalwood exported from western Australia prove that the wood finds ready markets, but whether the whole of the export is used in perfumery, carving, and for ceremonial purposes, or is used in part for the production of 'Indian' oil, it is impossible to say. In view of the decision of the Mysore government to increase its output of sandalwood oil and in

the end, as it would appear, to establish a virtual monopoly in Mysore oil, a demand for western Australian sandalwood is likely to arise in Europe. Sandalwood is getting scarce in and near the settled districts of western Australia, but the extent to which it still exists is not accurately known. The present supplies are largely drawn from the eastern goldfields areas, but it is understood that sandalwood has been found in mid-continent in the neighborhood traversed by the Trans-Australian Railway. The extent of the growth there has yet to be ascertained." The question of the composition of the oil derived from West Indian sandalwood is now under investigation at the Imperial Institute.

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## CURRENT LITERATURE.

### SCIENTIFIC AND TECHNICAL ABSTRACTS.

CYANOGENETIC GLUCOSIDES IN FERNS.—Greshoff has demonstrated the presence of a cyanogenetic glucosides in *Pteris aquilina* L., in *Gymnogramma aurea* Desv., and in species of *Lastræa* and *Athyrium*. Mirande has found a cyanogenetic glucoside in *Cystopteris alpina* Desv. It is present in all the green parts of the plants in fairly large quantity in the spring, but gradually diminishing as the season advances. (*L'Union Pharm.*, 59, 371, from *The Pharm. Jour. and Pharmacist*, May 31, 1919.)

ALKALOIDAL VALUATION OF EXTRACT OF BELLADONNA.—Differences having arisen regarding the alkaloidal value of extract of belladonna as determined by French and English analysts, it is desirable that a uniform method should be internationally adopted. The authors show that the process of the British Pharmacopœia (1898) involves losses due to incomplete removal of the alkaloids during the process of shaking out, to the numerous manipulations, and to the drying at 100°, by which a volatile alkaloid is driven off. Preference is given to the process of the French Pharmacopœia, which is simpler and determines the *total alkaloid*.—Goris and Beausite. (*Bull. des Sciences Pharm.*, 26, 53, from *The Pharm. Jour. and Pharmacist*, May 31, 1919.)

MICRO-DETECTION OF LIGNEOUS ELEMENTS IN FLOURS AND PASTRY.—It is difficult to identify starch grains in cooked flours



and pastry, on account of the distortion of the starch by the action of the heat to which the articles have been exposed in cooking. In such cases the ligneous elements will often afford valuable evidence as to the nature of the starchy material originally used. The following method enables these elements to be isolated in a condition favorable for micro-examination. About 0.5 Gm. of the flour or pastry is well agitated with 10 mls of 10 per cent. nitric acid, and heated, first on the water-bath for five minutes, then for one minute directly in the flame. The heated mixture is centrifugated and the liquid decanted. The residue is boiled with 5 mls of 10 per cent. caustic soda solution, diluted with 5 to 10 mls of water. After again centrifugating the deposit is suitable for examination. If the pastry is rich in fat this should first be removed by means of suitable solvents, and the fat-free residue treated as above.—T. Fellenberg (*Mitt. geb. Lebensmitt u. Hygiene; Annales Chim. Analyt.*, 1919 (2), 1, 163, from *The Pharm. Jour. and Pharmacist*, May 31, 1919.)

ANTINEURITIC VITAMIN IN WHEAT AND CORN KERNEL.—According to Voegtlin and Myers the germ or embryo of the wheat and corn kernel contains all of the antineuritic vitamin of these cereals. Wheat flour or corn meal containing the germ is, therefore, more nutritious than the correspondingly highly milled products. Consideration of the distribution of the antineuritic substance in the wheat and corn kernel and in the animal body suggest that this accessory food is necessary for the metabolism of the growing plant as well as the animal body. It appears that cells with an especially active metabolism are also rich in antineuritic vitamin. (*Amer. Journal of Physiology*, from *Jour. Amer. Med. Asso.*, June 21, 1919.)

ESTIMATION OF THE NUCLEIN CONTENT OF YEAST.—C. A. Lubsen (*Pharm. Week-blad.*, 1918, 55 (50), 1625-1628; through *J. Chem. Soc.*, 1919, 115, ii., 124).—In analyzing foodstuffs for nuclein content, pepsin-hydrochloric acid hydrolysis is employed (in which the nucleo-proteins are insoluble) to remove other proteins. The nucleins are then determined in the residue by estimating the phosphoric acid, which constitutes 4 to 7 per cent. of the nucleo-protein. The strength of the hydrochloric acid is of importance, for, if it be only 0.1 per cent., low results are obtained, but accurate results are yielded by 0.24 and even 0.35 per cent. acid, showing

that with acid of this strength the nucleins are not further hydrolyzed, as was suggested by some workers. H. F. E. H. (*The Analyst*, May, 1919).

IODIMETRIC ESTIMATION OF ACETONE.—W. Marriott (*J. Biol. Chem.*, 1918, 16, 281; through *J. Pharm. Chim.*, 1919, 19, 133-136).—With reference to the method described by Shaffer and Marriot (*Analyst*, 1914, 39, 184) for the estimation of acetone and B-hydroxybutyric acid in urine, in which use is made of Messinger's method for the estimation of acetone, the following work was done to control the accuracy of that method: A sample of acetone regenerated from the bisulphite compound was purified by distillation with permanganate and then with calcium chloride. The product was then submitted to fractional distillation, and the fraction distilling at 56° to 75° C. collected. Very considerable care is required in making up and manipulating dilute aqueous solutions of acetone. The sample is weighed out in a small glass bulb of 2 to 3 Cc. capacity. The bulb is dropped into a 2-liter measuring flask and broken under water, the solution being then made up to the mark. Precautions are required to prevent loss of acetone in measuring off this dilute solution for analysis. The flask is closed by a rubber stopper with two holes, through one of which is passed a 25 Cc. pipette. The pipette is filled by means of a rubber ball, and the measured liquid is transferred to a flask containing 500 Cc. of water, the point of the pipette being dipped below the surface of the water. To this solution 50 Cc. of N/10 iodine and 10 Cc. of caustic soda solution at 60 Gms. per 100 Cc. are added. The flask is corked, shaken, and allowed to remain for five to ten minutes; 15 Cc. of hydrochloric acid are added, and the liberated iodine is titrated with N/10 thio-sulphate. Each Cc. of N/10 iodine consumed is equivalent to 0.000968 Gm. of acetone. The results are quite sufficiently accurate: for instance, acetone taken 30.62 Mgrms., found 30.64 Mgrms.; taken 20.95, found 21.09 Mgrms. Geelmuyden has stated that small quantities of acetone cannot be distilled from aqueous liquids without appreciable loss; the author has proved that, with suitable precautions, acetone can be distilled and collected quantitatively in a few minutes. Five hundred Cc. of an aqueous solution containing 33.7 Mgrms. of acetone determined by the above method were placed in a Kjeldhal distillation flask of 800 Cc. capacity, with a tin

condenser terminating in a glass tube dipping below the surface of 50 Cc. of water placed in a receiver. Distillation was continued for thirty minutes, but it was ascertained, by titrations made at intervals, that the whole of the acetone had distilled over after ten minutes, the distillate then containing 33.6 Mgrms. of acetone by the Messinger method. The losses recorded by Geelmuyden did not occur, and it is suggested that that author did not have the end of the condenser dipping below the water in the receiver. (*The Analyst*, May, 1919.)

NEW URINARY REAGENTS.—The following reagent is said to furnish a very delicate test 1 : 1,000,000) for albumin. Added to urine it produces a white ring at the junction of the liquids (*Il Policlinico*, Mar., 1918):

Potassium bichromate .....	10 Gm.
Dilute sulphuric acid (25 per cent.).....	100 Drops
Glacial acetic acid .....	100 Drops
Distilled water .....	100 Gm.

A copper-phosphate mixture is recommended by Folin and McEllroy (*Jour. Biol. Chem.*, 1918, 33, 513) as a reagent for sugar. They claim for the alkaline phosphates the advantages that they are cheaper, that they do not themselves reduce sugar, and that they tend to regulate the degree of alkalinity at a lower level of hydroxyl ion concentration than is obtained by carbonates alone. The mixture is as reliable as Benedict's reagent and rather more prompt. Its formula is as follows:

Sodium pyrophosphates .....	100 Gm.
Crystallized disodium phosphate .....	30 Gm.
Sodium carbonate .....	50 Gm.
Water .....	1 Liter

To this add:—

Copper sulphate ( $\text{CuSO}_4, 5\text{H}_2\text{O}$ ) .....	13 Gm.
Water .....	200 C.c.

(From *The Prescriber*, September, 1919.)

OXIDATION OF APOMORPHINE.—It has already been shown that when morphine is digested with unsterilized food substances no apomorphine is produced, nor is such the case with ferments in the



presence of chloroform, toluol or sodium fluoride. Experiments with fungi and bacteria have shown that neither *Aspergillus* nor *Pencillium* splits up cocaine with formation of an oil with a basic reaction, probably pyrrol derivation; in no case, however, was benzoic acid produced; bacteria, on the other hand, readily do so. Neither fungus produces apomorphine from morphine. Apomorphine hydrochloride yields by oxidation with dilute solution of potassium ferricyanide a substance soluble in benzol with production of an intense amethyst-violet color; this is an exceedingly delicate test for apomorphine. By a rather lengthy process (details in the original), an oxidation product was obtained in absolutely black crystals soluble in chloroform with intense violet color similar to that produced when an apomorphine solution is carefully oxidized with potassium bichromate and shaken with chloroform. (E. Winterstem, *Schweiz. Apoth. Ztg.*, 57, 133. From *The Pharm. Jour. and Pharmacist*, July 5, 1919.)

DETERMINATION OF ACIDS IN GASTRIC JUICE.—Binet and Verpy describe a technic which is based on Gaultier's simplification of Robin's modification of Töpfer's method. They commend the simplicity and the rapidity of the technic. It shows by three changes of tint in the one specimen of gastric juice in the single tube the content in the gastric juice of the hydrochloric acid, of the acids of fermentation, and of the total acidity. This is accomplished by adding a 0.548 per cent. solution of soda (137 Cc. of normal sodium hydroxid with water to 1 liter). The tube of 1.5 Cm. caliber is graduated in tenths of cubic centimeters to a height of 15 Cc. above the first mark, which represents a capacity of 5 Cc. Two other reagents are required: a 2 per cent. alcoholic solution of phenolphthalein, and Töpfer's reagent, which is a 0.5 per cent. alcoholic solution of dimethylamidoazobenzol. The filtered gastric juice is poured into the tube to the 5 Cc. mark; then one drop of the phenolphthalein solution and one drop of the Töpfer. If there is free hydrochloric acid present, the fluid turns a cherry red. Then with a dropper the titrated solution of soda is added, agitating at each drop, until the fluid turns the color of mandarin orange juice. This indicates saturation of the HCl and the figure marked on the tube represents the weight of free HCl in a liter of gastric juice. The soda solution is added further, drop by drop, until the tint veers to a distinct yellow. The figure representing the free HCl is then subtracted from the

figure reached now by the fluid, and the difference represents the acids of fermentation present. The soda solution is then added further, drop by drop, until the tint turns slightly pinkish. The mark then reached represents the total acidity. By subtracting from this figure the sum of the two other figures, we get the figure for the HCl in organic combinations. Comparative tests with this technic have confirmed its reliability, and it is in constant use in Leoper's service. (From *Jour. American Med. Assoc.*, Sept. 13, 1919.)

## MEDICAL AND PHARMACEUTICAL NOTES.

*Chloramine Paste*.—A formula for chloramine paste is given by A. Carrel in his recent work, "The Treatment of Infected Wounds." It is as follows:

Chloramine-T .....	10
Stearate of soda .....	70
Water .....	1,000

The preparation of this substance is somewhat difficult, and it should be made by means of a mechanical mixer in order to obtain a thoroughly homogeneous paste. (From *The Prescriber*, August, 1919.)

*Chloramine Ointment*.—The following ointment is recommended by B. Deplas (*Presse médicale*) as a useful antiseptic application for superficial wounds:

Virgin wax .....	100	Gm.
Olive oil, sterilized .....	200	"
Balsam of Peru .....	3	"
Tincture of benzoin .....	3	"
Chloramine-T .....	4.5	"

Chloramine Surgical Powder:

Chloramine-T .....	1	Gm.
Zinc stearate .....	10	"
Sodium stearate .....	89	"

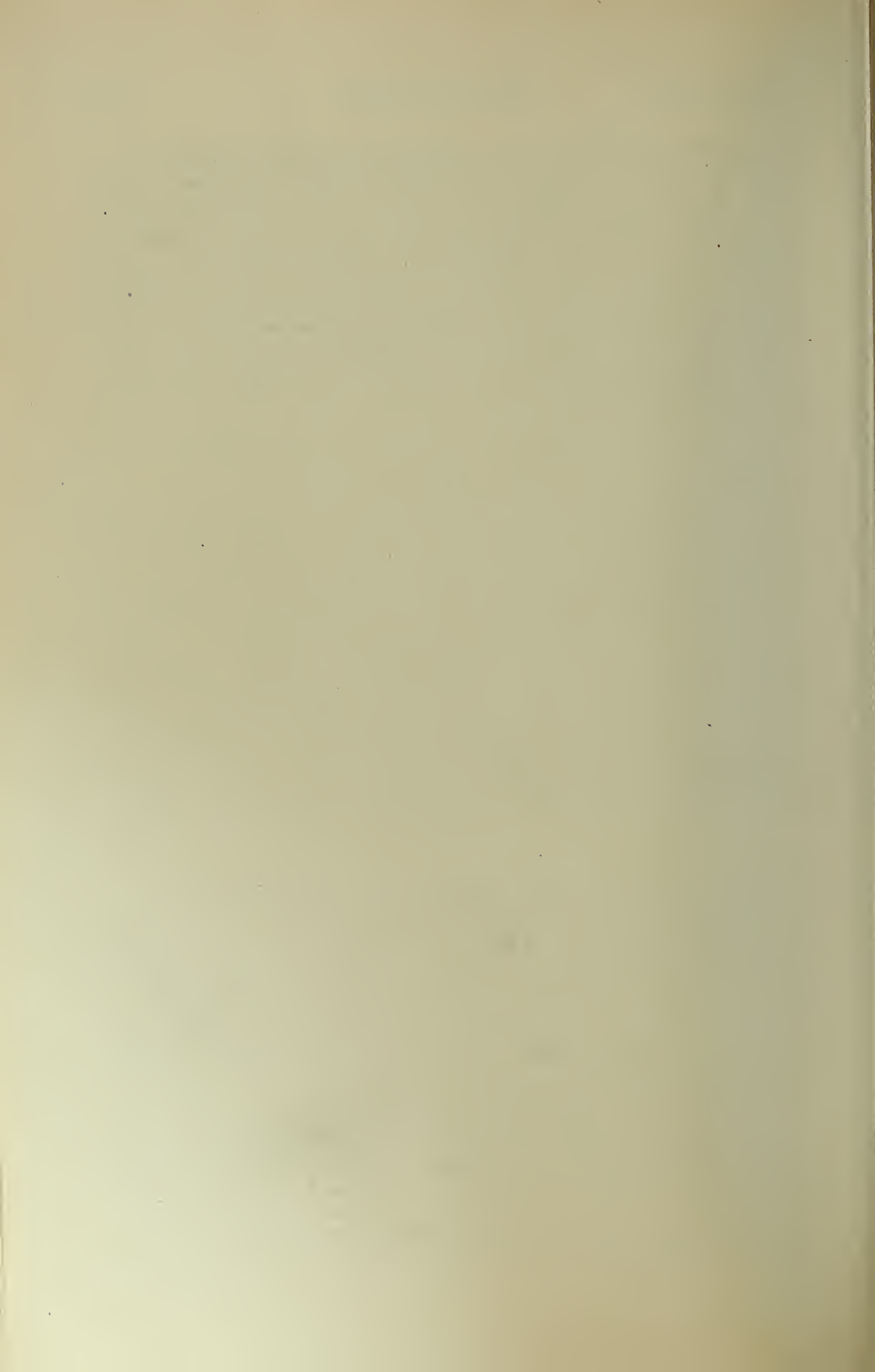
(From *The Prescriber*, August, 1919.)

*Sugar Treatment of Tuberculosis.*—In the last issue we printed several abstracts on the treatment of tuberculosis by means of sugar injections, a subject that is at present exciting lively interest in Continental practice. From there it has spread to America, where it is being given a thorough trial by several National Boards of Health. The treatment has been under trial by Prof. Le Monaco of Rome since 1907, and the following comment, which appears in a recent issue of *Riforma Medica* (Naples), is interesting: "The advantages of this new medication of the bronchi are truly notable, in addition to the fact that it avoids disturbing the gastro-intestinal functions, which is such a frequent drawback to the administration of drugs to act on the expectoration. The sugar treatment can be continued as long as desired, because it is harmless, to say nothing of the advantages of the sugar as a source for energy, developing a goodly number of calories in the intra-organic metabolism. In the tuberculous this method treatment is of preëminent importance, because even in the gravest cases it reduces the bronchial secretion, and thus diminishes the cough and the annoying night sweats. On the side of prophylaxis, this new remedy is destined to prove useful likewise, as, if the expectoration is diminished, there will not be so much sputum scattered about, and hence there will not be so much chance of contagion from this vehicle of infection, the most dangerous and the most certain of all." Further developments of this promising method will be awaited with interest. (From *The Prescriber*, July, 1919.)

INCOMPATIBILITY OF MERCURIC BENZOATE AND SODIUM CHLORIDE.—Gaucher and other Continental physicians have prescribed mercuric benzoate dissolved in dilute sodium chloride solution for administration by hypodermic injection for the treatment of syphilis. At a recent meeting of the Académie de Médecine, E. Seger pointed out that such a combination was incompatible, and that mercuric chloride and sodium benzoate resulted from the double decomposition of these salts. M. Delépine fully confirms this. He prepared two solutions, one with mercuric benzoate and sodium chloride, according to Gaucher's formula; the other with equivalent quantities of mercuric chloride, sodium benzoate and sodium chloride. The ultimate composition of the two products was identical. On shaking out with ether, that solvent contained the same amount of mercuric chloride in each case. This proves that the original formula



of Gaucher is defective, and that nothing is gained by the use of mercuric benzoate, to immediately decompose it into mercuric chloride. If ammonium benzoate is used instead of sodium chloride in the solution with mercuric benzoate and some ammonia, the result is different. A crystalline double salt is formed, which might possibly be of service therapeutically. Ultimately, however, even this compound is likely to be decomposed into mercuric chloride when it comes into contact with the sodium chloride present in the body. (M. Delépine, *Repertoire Pharm.*, 1919, 30, 184. From *The Pharm. Jour. and Pharmacist.*)



# THE AMERICAN JOURNAL OF PHARMACY

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## EDITORIAL.

### PHARMACISTS AND THE PROHIBITION ENFORCE- MENT LAW.

The National Prohibition Enforcement Act and the regulations (T. D. 2940) issued by the Internal Revenue Bureau for the enforcement of this and the several Congressional enactments that were precursory thereto, have placed additional responsibilities upon the pharmacists of the United States. In anticipation of such action, the former president of the American Pharmaceutical Association recommended at the New York meeting that such added responsibilities "should be accepted as a tribute to the dignity and responsibility of the calling and as a recognition of the honesty and worthiness of the profession as a whole which is implied by such a trust." We have faith in the medical and pharmaceutical professions and believe that these on the whole will measure up fully to the responsibility.

Whatever the reasoning that actuated the framers of this law, its enactment has established beyond controversy several important principles. The use of distilled spirits and wines as medicines is clearly recognized as a proper use of non-beverage liquors and thus the limitations of T. D. 2788 which declared "that the withdrawal of whiskey, brandy, and other distilled spirits was presumed to be for *beverage purposes*" and not permissible under the War Prohibition Law and the further declaration therein that "it is not believed that there is any legitimate use for wines for medicinal purposes" are abrogated. Other distilled spirits for medicinal purposes, as well as alcohol, is thereby made available at the non-beverage excise tax of \$2.20 per proof gallon instead of the bever-



age spirit tax of \$6.40, and likewise vinous spirits that are prescribed as medicines or as vehicles for medicines.

The law very rightly now recognizes these "liquors" as medicinal substances to be prescribed only by a physician who holds a permit to prescribe liquors and is duly licensed to practice medicine and actively engaged in the practice of such profession, and in good faith as a medicine, after a careful examination of the person for whom the liquor is prescribed. In the future such prescriptions will, except in certain emergencies, have to be written on official forms supplied by the commissioner, serially numbered and with stubs on which copies of the prescriptions are to be kept and returned to the commissioner. Not more than a pint of spirituous liquor to be taken internally shall be prescribed for use by the same person within any period of ten days and no such prescription shall be filled more than once.

The compounding of these prescriptions must be by a pharmacist who has a permit under the Act and "who is duly licensed under the laws of his state to compound and dispense medicine." Here we have a Congressional recognition of the licensed pharmacist as the only person to compound and dispense medicine, a principle for which pharmacists have long contended.

While the enforcement of this law is left with the Treasury Department and its Bureau of Internal Revenue, it is apparent that it is no longer merely a question of revenue collection that is concerned. This Department has all the machinery necessary and many years of experience and many officials and employees trained in the methods of the distilling and wine industries and so the framing of regulations and the carrying into effect the provisions of the National Prohibition Act has been made a special feature and duty of the Commissioner of Internal Revenue, and it is understood that a new division composed of Federal Prohibition Enforcement Officers is to be created.

With the changes which time, education, and the advanced moral tone of our people have effected, the "liquor business" as a merchandising of alcoholic beverages is a thing of the past and the "liquor dealer" has ceased to exist. This law does not mention such, but makes it a part of the professional duty of the pharmacist to dispense alcoholic medicines in accordance with regulations which minimize the possibility of the infraction of the law. It also recog-

nizes that alcohol is indispensable in the preparation and preservation of many medicines. The dispensing of distilled and vinous liquors as medicines is thus recognized as a distinctly professional duty of the pharmacists and of no other class and as a necessary non-beverage use of these. It would follow that the necessity for the classification of "Retail Liquor Dealer" had ceased to exist in the Treasury Department. The pharmacist under this permit can never become a dealer in or dispenser of beverage spirits and his classification under this objectionable title is now, more than ever before, incongruous and should be forthwith discontinued by direction of the Department as inconsistent with the law and the regulations.

The regulations, T. D. 2940, that have been framed by the Department for the enforcement of the National Prohibition Act and the several preceding acts known as the Food Control Act, the War Prohibition Act and the Revenue Law of 1918 contain many features that will have to be carefully studied by pharmacists in order that they may comply therewith. As we now view these, it would seem that it may prove a hardship if not impracticable to literally comply with some of the most exacting.

All persons who desire to use for manufacturing purposes or to sell distilled spirits or wines for medicinal or non-beverage purposes will be required to file an application in triplicate with the Prohibition Enforcement Officer of the State in which the business is to be conducted which must be approved by the Commissioner of Internal Revenue and likewise a bond in duplicate to be approved by the said Prohibition Enforcement Officer. The minimum amount of the bond is to be \$1,000, the maximum \$100,000 in accordance with quantity of liquors purchased. All permits issued prior to November, 1919, will have to be renewed under the amended form and the permit must receive the approval of the Commissioner and all holders of these permits are required to give a new bond not later than December 1, 1919.

The new form of application for permit contains several new features. Paragraph (b) in this provides for a statement regarding each preparation that is neither U. S. P. or N. F., requiring the name of the preparation, for whom manufactured, per cent. of alcohol by volume, and each of these preparations must have the approval of the Commissioner. When new special formulas or preparations are

manufactured in excess of five gallons within a period of 90 days, a separate or supplemental permit must be obtained. The formula and process of each of these non-official preparations, upon request, are to be furnished the Commissioner for approval before permit is approved. This provision will be somewhat of a hardship to the manufacturing pharmaceutical houses who list a long line of unofficial fluid extracts, tinctures, elixirs and specialties made either for their own sales or very frequently as private formulas for druggists, physicians, or for proprietary medicine dealers.

A duly licensed practitioner of medicine may secure a permit without giving bond for the purchase of not exceeding two quarts of alcohol or alcoholic preparations during a period of one year by filing the required application for permit and making sworn statement that such alcohol or alcoholic preparations are to be used in his practice. This is probably a concession to the homeopathic physicians who objected to the limitations placed upon the procuring of their tinctures and alcoholic dilutions under the regulations of T. D. 2788.

The law, under Title II, Section 4, states that medicinal preparations made in accordance with the formulas of the American Institute of Homeopathy that are unfit for beverage purposes, "shall not be subject to the provisions of this Act." Evidently the intent was to recognize the Homeopathic Pharmacopoeia of the United States, prepared by a committee of that body and published by the Institute, as the official authority for homeopathic remedies. The mention thus made in the same sentence as are named the United States Pharmacopoeia and the National Formulary would indicate that a standing or recognition of these three as coequal as standards for the formulas contained was what was intended by the law. Under these conditions it is rather singular that the regulations fail to mention the Homeopathic Pharmacopoeia or to make any reservations concerning the medicines used especially by that school.

It is noteworthy that in these proposed regulations the Department has promulgated standards for alcoholic preparations in which non-beverage alcohol may be used. Paragraph (a) of these states that "U. S. P. and N. F. preparations, except such as may be designated by the Commissioner as suitable for use as a beverage or which have no legitimate use as a vehicle." This certainly places



rather remarkable responsibility and assumption of authority upon the Commissioner, who presumably is not a medical man, to determine what the medical practitioners of the country shall be permitted to prescribe as remedial agents or as vehicles for such remedies. The scope of the Pharmacopœia is limited solely to substances and formulas "which are used for medicinal purposes," and the judgment of the Committee of Revision composed of practitioners and scientific workers in this special field, should not be set aside by the precipitate opinion of an official.

Paragraph (b) of these standards attempts to define a *medicine* under this law, that term not being defined in the Act itself. The definition given is: "(b) Any medicinal preparation will be classed as a medicine, provided the same is unfit for use as a beverage, and contains no more alcohol than is necessary for the purpose of extraction, solution or preservation, and contains in each fluid ounce a dose as a whole or in compatible combination of one or more agents of recognized therapeutic value, and contains no agents either chemically or physiologically incompatible with the active medicinal agents upon which the medicinal claims are based." The wording of this paragraph is unfortunate. The adjective "medicinal" applied to a preparation stamps such as having the properties and uses of a medicine. A "medicinal preparation" is incontrovertibly a "medicine" and a declaration of a department cannot change its status. A medicine is a medicine as much as "pigs are pigs."

Again who is to determine which of the "agents" are "of recognized therapeutic value"? There is a wide diversity of opinion among able medical practitioners as to "therapeutic value" of many of the remedial agents that are extensively employed and where the doctors differ among themselves would it be safe to accept the dictum of a non-medical department? In a "compatible combination" may not even the alcohol contained be one of the "agents of recognized therapeutic value"?

When we stop to consider the innumerable chemical and physiological incompatibilities possible and the many times that either accidentally or intentionally these are evidenced in the prescriptions of the most learned and skilled physicians we must conclude that the department is promulgating an impracticability bordering on the verge of the ridiculous and which must, necessarily, be observed

very frequently in the breach. In this paragraph, in assuming authority to interpret the propriety of medical customs and practices, the Department is treading upon dangerous ground in which, for the welfare of the people, it would be well not to be too aggressive.

In the establishing in this portion of the regulations definitions and standards for flavoring extracts, the Bureau of Internal Revenue is taking another advanced step and one which, when the Food and Drugs Act was under consideration, Congress declined to sanction. The attitude of Congress at that time was that the duty of a Department of the Government was administrative, to enforce the laws, and not to make them; that a department should not be given the authority to make the standards for the articles of food and drug consumption which it was to be entrusted to pass upon in its enforcement of the law; that it should not be empowered thus to act in the dual capacity of law maker and enforcer. It is an open question whether public opinion and legislative sentiment have since changed to warrant now the departure from that attitude.

A flavoring extract is defined "as a solution, in ethyl alcohol of *proper* strength, of the sapid and odorous principles derived from an aromatic plant, with or without its coloring matter, and conforms in name to the plant used in its preparation." It is to be observed that if any coloring is used in these preparations it must be the natural coloring matter of the plant named. This eliminates the use in these of artificial coloring of any kind or character. Standards are named for twenty-three flavoring extracts, a differentiation being made between extracts of cassia and cinnamon and between anise and star anise extracts. Tincture of ginger is held to be a "medicinal preparation" and not a flavoring extract and must be made according to the U. S. P. and no standard is given for ginger extract.

The enormity of the task that has been placed upon the Internal Revenue to enforce the recently enacted Narcotic and Prohibition Laws, which are more police measures than they are treasury enactments, calls for our sympathy and coöperation and our criticisms are intended as constructive aids. It is likewise the duty of the medical and pharmaceutical professions to assist faithfully, not only in the discharge of the responsibility placed upon them by these enactments, but also to sustain and uphold the spirit of these laws and to

support the officials in their enforcement. Nevertheless Congress in its lawmaking and the Departments in the framing of regulations should obtain the advice of the professions or trade interests that are directly concerned. If this co-operation was sought and advice accepted many of the inconsistencies could be avoided. The legislation and the regulations here commented upon are practical illustrations of the impracticabilities that result from the ignoring of such a common-sense principle.

G. M. B.

### PHARMACEUTICAL PESSIMISM.

In a recent letter to the editor, a valued correspondent wrote: "A friend of mine, who is in the advertising business, states that in reading the literature of pharmacy it is very pessimistic and so far he has been unable to obtain an optimistic view. This is quite the contrary to some of the writings he has read in regard to medicine, which have a tendency to glorify the profession."

This comment illustrates again "The Evil of Disparagement" to which attention was directed in our editorial column in the April issue. It is based upon the only too evident tendency among many pharmacists and likewise some American Pharmaceutical journals to disparage the work and position of pharmacy. This internal belittling of pharmacy is too often made the foundation for external criticism and the public's slight estimation of the pharmacists.

The fad of speaking disparagingly of pharmacists and their efforts should long ago have run its course in pharmaceutical circles. It cannot be too strongly condemned. The evil that it has already accomplished cannot be estimated, and the quotation above given is but another evidence of the impressions conveyed to those who are outside of pharmacy. It has been disheartening to the writer, at times, to have belittling and prejudicial statements from pharmaceutical publications offered by government officials, legislators and members of other professions as evidencing the true status of pharmacy.

It is unjust to the vocation that we represent, that the scientific attainments and many public services rendered to mankind by many eminent pharmacists in America as well as in other countries should be ignored and that the public should be given an absolute misconception of the part performed by pharmacy in the discharge of its duty to society as one of the branches of professional medicine.



Pharmaceutical journalists should certainly not be ignorant of the history of pharmacists and their contributions to science and public knowledge and welfare. Pharmaceutical journalism, at least, should be alive to the necessity for changing its attitude and for the edification of the public should not fail to present to the world the many services rendered by pharmacists as evidences of the good faith and professional standing of those who are conscientiously devoting their energies along pharmaceutical lines.

G. M. B.

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#### REPORT OF COMMITTEE ON PHARMACOPŒIAS AND FORMULARIES OF THE NEW JERSEY PHARMA- CEUTICAL ASSOCIATION.

Before the next annual meeting of the New Jersey Pharmaceutical Association, the convention called for the tenth decennial revision of the Pharmacopœia of the United States will most likely have been held in Washington and another committee of revision have been selected. Hence before this meeting adjourns accredited delegates to represent our State Association at that convention should be selected and their alternates named.

As the plans already adopted provide for the simultaneous revision of the National Formulary so that the fifth edition of that work shall be issued at about the same time as the U. S. P. X and both to become authoritative at the same date, it is, likewise, probable that the committee of revision of the Formulary will be appointed by the American Pharmaceutical Association before our meeting in 1920. Hence it is important that any recommendations relating to these revisions or any instructions to your delegates should be decided upon now.

The plan proposed by Dr. Lyman Spalding for the preparation of a "National Pharmacopœia" with but very little changes therein, has withstood the test of a century. It is truly American and democratic, and as we believe that it secures the most representative gathering of the interests that are concerned in the production of an authoritative materia medica that shall provide for the important needs of the entire country in this respect and supplies the very best talent that is needed for the selection of the Revision Committee, we recommend that this Association endorse a continuation of this plan for the revision of the U. S. P.

It is noteworthy that while the U. S. P. IX has now been before the public for three years, the criticisms and suggestions for improvements and the actual errors pointed out, have been very much less than occurred within the same period after the revisions of 1880, 1890 and 1900. Like all other works of human beings, it has its faults and corrections as well as the changes that have occurred in the medical practices and in the materia medica since 1910, call for the usual decennial revision.

It is believed that the Committee of Revision and the Pharmacopœial Convention will welcome constructive criticisms and suggestions. At the previous convention, your delegates presented in book form a typewritten abstract of all recommendations relating to the Pharmacopœia that had been printed in the proceedings of the New Jersey Pharmaceutical Association during the decade. This was referred to the Committee of Revision and no doubt was of some service in their work. We would recommend that the delegates selected to attend the 1920 convention be instructed to prepare and submit a similar report embodying abstracts from our proceedings and the suggestions and recommendations approved at this meeting.

Your committee are of the opinion that this Association, as well as other pharmaceutical, medical and chemical societies, should enunciate its views upon the general principles that should be followed in the coming revision and likewise upon special topics. With that end in view, we submit the following specific recommendations.

We recommend that the "Scope of the Pharmacopœia" as defined in the U. S. P. IX be retained for the next revision.

We recommend that the admission of an article or preparation to the pharmacopœia be based upon its determined general medical use justifying an official standard. That the dismissal of any article now standardized as a medicament in the U. S. P. IX be based upon a determination that its general use as a medicine is not sufficient to justify its retention.

It is believed that the monographic presentation of standards for the drugs, chemicals and preparations in alphabetical sequence as followed in the preceding revision is the best that can be devised both for reference and clarity of presentation of the subjects and it is recommended that this be continued.

It is especially recommended that the style adopted for titles, synonyms, definitions and "purity rubric" in the ninth revision be

followed in the tenth and that limits of purity in each case be given careful consideration and made as elastic as is consistent with the maintenance of standards of quality and the prevention of fraud and carelessness.

With the changes that are continuously taking place in the source of and markets for pure drugs and also the numerous undertakings throughout the world of the cultivation of drug plants, it is urged that unless absolutely necessary in order to determine quality, the Pharmacopœia omit geographical designations and further that such changes as are due to cultivation, difference in climates or modes of collection and preparation of such drugs be given due consideration in the framing of the standards and tests.

While approving of the principle of the unification of formulas for potent remedies by international agreements, it is our opinion that the conclusions arrived at by the "Conférence Internationale pour l'Unification de la Formule des Médicaments Héroïques" held in Brussels in 1902 were not entirely free from faults and that these are not such as would be approved in their entirety at this time. It is recommended that the United States Pharmacopœial Convention should take the initiative in inviting another international conference for this purpose in the near future, preferably, in the United States and that the conclusions be incorporated in the U. S. P. X.

It is believed that the method of stating the chemical formulas adopted in the ninth revision is well suited for the purposes of the pharmacopœia and so it is recommended that the same methods or with only minor modifications, be retained. Also that the atomic and molecular weights employed be the latest available Report of the International Committee on Atomic Weights.

It is recommended that the weights and measures adopted be restricted exclusively to the metric system. In order that the professional interests may be encouraged and likewise that the commerce of the nation may be stimulated it is urged that the Pharmacopœial Convention give the force of its endorsement toward making the use of the metric system universal in medical practices and in the commercial transactions in the United States after a fixed date.

In the eighth and ninth revisions 25° C. was adopted as the standard temperature. The Bureau of Standards of the United States has persisted in maintaining 20° C. and several of the other departments of the federal government prefer to follow the Bureau in this matter. It is obvious that two standard temperatures should



not exist in this country and we have come to the conclusion that 20° C. more nearly represents the normal room temperature in the various sections of the United States and we recommend that in the future revisions 20° C. be adopted for the standard temperature except where in a few determinations, such as those of refractive indices, another temperature may be necessary and that in each such group of necessary variation the temperature to be adopted shall be stated if it varies from the standard.

In order to economize the space and the cost of publication, the U. S. P. IX introduced a plan for general formulas which was tested out in the type formulas given for fluid extracts and for tinctures. This plan has eliminated much useless repetition and appears to have worked entirely satisfactorily and we recommend its extended use wherever practicable in other classes of official preparations.

The previous pharmacopœial convention "recommended that a range of volume content of absolute alcohol be stated in the Pharmacopœia for each preparation containing alcohol." While the recommendation was not carried out in its entirety a partial table of alcoholic content was published in Part II. The importance of such official statements of the range of alcoholic content permissible in each official preparation is apparent to every pharmacist and would be a guide to those entrusted with the enforcement of the laws against adulteration of drugs. It is therefore recommended that wherever possible the U. S. P. IX should give such information.

The necessity for accuracy in the preparation of medicines and in their administration needs no argument. It is recommended that the U. S. P. define and describe standard graduate measures and a standard dosage measure.

The enormously increased use of "biologic products" such as serums and bacterins in medical practice must be recognized. The same is also true regarding the use of many animal organ drugs such as mammary substance, ovarian substance, corpus luteum. It is recommended that especial consideration be given to the necessity for official standards for these.

The Federal Food and Drugs Act fails to recognize any standard for homeopathic drugs and so far the homeopaths have failed in their endeavors to have Congress recognize as a legal authority the Homeopathic Pharmacopœia of the United States and as the coequal of the U. S. P. and N. F. The reason for thus failing to recognize

an authoritative legal standard for homeopathic remedies which are necessarily prepared by different methods from those of the present U. S. P. or N. F. need not be discussed in this report. It is well known that in some sections of the United States, homeopathic drugs have a large use and are sold by many druggists, and legal standards for such that are commonly sold and used should be established and designated by the law. We are of the opinion that the need for standards for homeopathic medicines can at least be met in part by a unification of the pharmacopœial standards. In the ninth revision of the U. S. P. certain innovations were introduced such as the chapters on "Biologic Assays," "Sterilization," and "Diagnostical Reagents and Clinical Tests." It would appear as no greater innovation for the tenth revision to have chapters such as appear in homeopathic pharmacopœias on "Cleansing of Utensils," "Vehicles," "Selection of Medicinal Substances," "Preparation of Potencies and Dilutions." The various classes of preparations used especially in homeopathic practice, such as mother tinctures or fresh drug tinctures, solutions, triturations, etc., could very likely be treated by general formulas. Representation of the Homeopathic Societies in the Convention and a Subcommittee on Homeopathic Standards of the Revision Committee, would readily provide for this part of the revision.

Regarding the revision of the National Formulary, we are of the opinion that the time is ripe for the coöperation of a committee of active medical practitioners in the edition to be soon undertaken. Such a coöperation of the medical societies should be solicited by the American Pharmaceutical Association which owns and controls this publication and should be given by the formation of a committee composed of practicing physicians acquainted with medical customs and usages. In close coöperation with a committee of revision composed of those whose experience and ability as pharmacists should be exceptional, medical assistance would be of great value in simplifying combinations and eliminating a number of the unnecessary and duplicating formulas. Moreover, it should stimulate the acquaintance of the physicians with the various useful preparations in the book and their increased prescribing of these to the advantage alike of the patient and the professions of medicine and pharmacy.

Despite the efforts of the various propaganda to popularize the Pharmacopœia and the National Formulary, it remains still a fact that comparatively few of the physicians are to-day sufficiently ac-

quainted with the formulas of either. Undoubtedly, this is very largely due to the fact that the physician is not as a rule interested in the mass of matter relating to standards and tests that is necessarily contained in these publications. An official epitome of each of these legal standard authorities should be prepared by a joint committee of physicians and pharmacists and these be widely distributed as mediums of education. Such epitomes should present in a readable way the information relating to composition, doses, practical uses and combinations that appeal to the busy practitioner. It must not be made a commentary or an unwieldy dissertation. It is believed that without surrendering in the least the dignity of authority or of position such epitomes of the U. S. P. and of the N. F. can be prepared and would go a long way toward overcoming the indifference of the medical practitioners and too often evident lack of acquaintance with the official *materia medica*.

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## THE ANATOMY OF UMBELLIFEROUS FRUITS.<sup>1</sup>

In a series of articles published in the *Schweizerische Apotheker-Zeitung*, Vol. 57, No. 13, pp. 183-188, Joseph Styger describes the macromorphology and micromorphology of a number of umbelliferous fruits. In the first of these articles the author discusses the structure of *Ænanthe Phellandrium* Lam., *O. Lachenalii* Gmel., *O. pimpinelloidea*, *Æthusa Cynapium* L. and *Levisticum officinale* Koch. as well as the distribution of the first and last named plants. The salient features of these articles are hereby presented:

*Ænanthe Phellandrium* Lam. The home of this species, commonly known as "Water Fennel," is Europe and Central Asia. The fruits are glabrous, up to 5 Mm. long, 2 Mm. broad and 1.5 Mm. deep, roundish-cylindrical, slightly laterally compressed, yellowish-brown, somewhat acuminate toward the style, crowned with the stylar cushion and sometimes with the bent style. Ribs broad, slightly projecting, the grooves being small and darker than those whose fruits are not so readily split. Under a hand lens the schizocarp is compressed dorsally, the fruit wall being very broad. The broad ribs are slightly projecting, the marginal ribs are strongly built; dorsal surface 1-stripped, commissural surface 2-stripped. The

<sup>1</sup> Abstract prepared by Prof. Heber W. Youngken.



endosperm is rounded dorsally, somewhat pressed in by the vittæ, on the inner side almost straight; sclerenchyma fibers run at the base of the ribs.

Under the microscope, the upper surface shows tangentially stretched cells with a slightly thickened cuticle. Beneath the epidermis of older fruits lies a parenchyma zone which is collapsed or compressed toward the inner part. The middle portion of the mesocarp is divided into two distinctly demarkated zones. The outer is composed of large, rounded, punctated, thick-walled parenchyma cells which take the red color with phloroglucin and hydrochloric acid, only over the vittæ lies a zone of unthickened collapsed tissue; on the commissural side, the punctuated tissue is small and round celled. The inner part is filled up with strongly lignified sclerenchyma fibers which are especially broad in the ribs (up to six rows of cells thick) and are extended in an almost interrupted row around the oil tubes. A similar patch, also, lines in the region of the raphe, but is not prolonged over the secretory passages. Only the marginal rib-plates stretch over almost half of the vittæ. The bast fibers are long-pointed, with small elliptical pores sloping to the left. The pitted trachea lie on the boundary between the sclerenchyma plates and the thickened parenchyma and are accompanied by thick-walled wood parenchyma. The secretory passages are roundish-oval, up to  $110\mu$  in lengthwise view and  $60\mu$  in transverse view; on the commissural surface they are for the greater part larger (up to  $180\mu$  in longitudinal section and  $90\mu$  in cross section). They border on the inner epidermis and are surrounded by well built, quadrate or weakly peripherally stretched epithelial cells. The seed coat is greatly collapsed, brown-walled, underdeveloped on the commissural surface. The thin-walled endosperm contains fixed oil and aleurone. Other *Ænanthe* species resemble this one and are differentiated in anatomical structures by the arrangement of the sclerenchyma elements and the wood parenchyma.

*Ænanthe Lachenalii* Gmel.—The thickened wood parenchyma is found only in the ribs, not in the inter-rib regions. The sclerenchyma fibers are arranged as in *O. Phellandrium*.

*Ænanthe pimpinelloidea*.—As in *O. Phellandrium* the sclerenchyma plates are more broadly developed in the ribs, but are extended over the vittæ in a more layered band, up to four rows broad.

*Æthusa Cynapium* L.—The fruit of "Fools Parsley" is oval, 4 Mm. long, 2.5 Mm. deep and 2 Mm. broad, pale yellow, crowned

with the styler cushion and both styles, very slightly cleft. The ribs are somewhat broad, the grooves strongly crowded together. These are pervaded through their entire length by dark-brown oil passages, which are especially prominent in the dorsal region and extend in arcuate fashion.

As examined with a hand lens, cross sections show the fruit wall to be oval, only nearly straight on the partition surface. The ribs are broad and very strongly projected; both the marginal costal are, moreover, slightly winged. In the middle of the inter-rib regions is an oil reservoir with reddish-brown contents; on the commissural surface are two such secretory passages. The endosperm is rounded dorsally and slightly concave in the region of the raphe.

Under the microscope, the outer epidermal cells are slightly tangentially elongated, over the ribs quadratic. Especially here the outer membrane shows small warts, owing to the parallel cuticular striæ as observed in surface section. The endocarp shows tangentially elongated cells. The inner layer of the mesocarp ( $60\mu$  broad and up to 15 cell rows thick) is built of tangentially elongated, strongly compressed cells. The outermost are finely reticulately thickened and surround the fruit like a closed band. The outer broader zone of the middle region is filled up with loose, very thin walled parenchyma tissue. The broad ribs are almost completely filled up with finely reticulately thickened tissue which exhibits a rounded form; its cells are almost regularly polygonal, only those lying along the margin being peripherally elongated. At the site adjacent to the rib ends lies the vascular bundle with a few narrow spiral tracheæ which are only distinctly noticeable in longitudinal section. They are accompanied by narrow-lumened, obliquely punctated and long taper-ended bast fibers. All the thickened elements are lignified. Outside of the fibrovascular strand in each rib lies a small secondary oil reservoir and at times there is found another similar one alongside of the thickened tissue. In the middle of the inter-rib region, bounding the inner thickened mesocarp zone lies a rounded oval secretory channel with reddish-brown contents and from  $110\mu$  long to  $75\mu$  broad. Both of the vittæ in the commissural region are somewhat larger. The seed coat is brown-walled and strongly collapsed; only in the raphe portion is it somewhat broader developed and shows a bending in of the endosperm. The endosperm is uniformly thickened, contains fixed oil, aleurone and rosettes of calcium oxalate from  $2-5\mu$  in diameter. In the

epidermal cells are contained yellow flakes and crystals, often plume-shaped, which are readily soluble in KOH with a yellow color, but insoluble in chloral, alcohol, water and glycerin.

*Levisticum officinale* Koch.—The habitat of this species, commonly known as "Lovage," is unknown, apparently Southern Europe; moreover, it is doubtlessly unknown as growing wild. It is cultivated in large quantities in the province of Sachsen, in Thüringen, Holland and France, and considerably in the garden as a cooking aromatic.

The fruits are quite scissile, the schizocarp up to 7 Mm. long, 3.5 Mm. broad and 1.2 Mm. deep, yellow to dark brown, mostly straight, seldom only slightly bent, ovate-oblong, crowned with the broad styler cushion and at times also with the bent style. The ribs are small and project strongly outward. Under a hand lens, the somewhat dorsally compressed mericarp is stretched, on the commissural surface, almost straight. All the ribs are strongly marked; the border ribs are wing-like, the latero-dorsal ribs are moved toward the midrib, so that both sides of the section appear only very slightly concave. There is a vitta in the tissue between each two ribs on the dorsal side. The commissural side shows two vittæ. The endosperm is oval and shows a slight concavity on either side of the raphe.

Under the microscope, the outer margin of the fruit is composed of proportionately large, quadratic or, in part, of somewhat higher than broad epidermal cells whose outer membrane is very finely warty. The endocarp cells are small and elongated. The whole mesocarp is composed of thin-walled, hollow and large-celled parenchyma. The fibrovascular bundles occupy the middle region of the ribs and are especially thickened toward the outer and inner epidermis. The few spiral tracheæ are accompanied by long-pointed, narrow-lumened and obliquely punctated bast fibers. Bordering the inner epidermis lie the secretion reservoirs (vittæ) of elongated oval form,  $135\mu$  long and  $30\mu$  broad. The commissural vittæ are generally somewhat smaller. The dorsal vittæ can attain a length of  $195\mu$ . The outer part of the testa is alone well kept and show slightly tangentially elongated right-angled cells. The inner seed coat is collapsed. The nourishing tissue is uniformly slightly thickened and contains fixed oil and aleurone.



# RELATIVE SENSITIVENESS OF THE FEHLING, PHENYL-HYDRAZINE AND NYLANDER TESTS FOR THE DETECTION OF DEXTROSE IN URINE.

BY GEORGE E. ÉWE,  
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*Standard Material Employed in Tests.*—Merck's chemically pure dextrose rendered anhydrous at 40° C., dissolved in proper proportion in distilled water to make standard solutions of the various strengths employed in the tests. Since the experiments extended over several days fresh solutions were prepared each day.

*Nylander's Test.*—Formula: Rochelle salt 4 Gms. dissolved in 100 Cc. of 10 per cent. sodium hydroxide solution, warm and add 2 Gms. bismuth subnitrate.

*Application of Nylander's Test.*—One volume of reagent was added to 10 volumes of dextrose solution; the mixture then being heated for 5 minutes in boiling water. A black coloration was taken to indicate dextrose.

*Fehling's Test.*—Formula:

Copper sulphate (cryst.) .....	34.639 Gms.
Sod. hydroxide sol. (sp. gr. 1.120) .....	500 Cc.
Rochelle salt .....	173 Gms.
Water qs. ....	1000 Cc.

Dissolve copper sulphate in 100 Cc. warm water and dissolve the Rochelle salt in the sodium hydroxide solution. Mix these 2 solutions slowly and add enough distilled water to make a yield of 1,000 Cc.

*Application of Fehling's Test.*—The Fehling's solution was placed into a test tube up to about 1 inch from the bottom of the tube; the solution was brought to a boil and a few drops of the dextrose solution was added. The mixture was then boiled for a minute. If no apparent reduction was observed the dextrose was added in sufficient quantity to obtain a reaction but not in greater volume than the volume of Fehling solution employed in the test. In applying the test to the dextrose solutions having a percentage of 0.0625 per cent. or less equal volumes of the Fehling solution and

dextrose solution were employed, boiled for one minute and set aside for one half hour to allow any precipitate to settle.

In all the tests blanks were run on the Fehling solution using distilled water in place of the dextrose solutions.

*Phenyl-Hydrazine Test.*—Formula: A mixture of 1 Gm. Phenylhydrazine hydrochloride, 2 Gms. sodium acetate, and 10 Cc. water was shaken together and 2 drops of glacial acetic acid was added. The solution was again shaken well and then filtered clear. This reagent was prepared fresh daily in these experiments.

*Application of Phenyl-Hydrazine Test.*—Five Cc. of the reagent was added to 10 Cc. of the dextrose solution in a test tube. The tube was placed in a beaker of boiling water and the water was boiled for one hour. The tube was then removed from the boiling water and allowed to stand at room-temperature. The appearance of the characteristic crystals of phenyl-glucosazone in the test was taken as a positive reaction. In solutions of dextrose of 0.125 per cent. strength and above, the crystals were formed in the hot liquid in less than an hour from the beginning of the application of the heat. In solutions of 0.0625 per cent. and less, the crystals formed after boiling for one hour and allowing to cool for various periods of time.

*Keeping Qualities of Phenyl-Hydrazine Test Solution for the Detection of Dextrose in Urine.*—Phenyl-hydrazine test solution is not a perfectly stable solution, but possesses much greater stability than it is usually credited with. The following experiments tend to prove this:

A quantity of the test solution was prepared as mentioned above and placed in an amber-glass bottle equipped with a ground-glass stopper. This supply of solution was kept at room temperature for 19 days and tested for sensitiveness at various times during that period. The results of these tests follow:

Strength of Dextrose Solution	Age of Test Solution	Reaction
0.005 per cent. ....	Fresh.	Positive after cooling and standing 45 min.
0.005 per cent. ....	2 days.	Positive after cooling and standing 55 min.
0.005 per cent. ....	6 days.	Positive after cooling and standing 75 min.
0.005 per cent. ....	10 days.	Positive after cooling and standing 90 min.
0.005 per cent. ....	19 days.	Negative after cooling and standing 24 hrs.

The comparative sensitiveness of the three tests for the detection of dextrose in urine are shown in the following table:

Strength of Dextrose Sol. (Percentage).	Phenyl-Hydrazine Test.	Fehling's Test.	Nylander's Test.
0.5 . . . .	Positive before cooling.	Positive while hot.	Positive (black coloration).
0.25 . . . .	" " "	" " "	Positive (brown coloration).
0.125 . . .	" " "	" " "	Positive (light brown coloration).
0.0625 . .	" after "	" " "	Positive (very light brownish).
0.06 . . . .	" " "	" " "	Negative.
0.03125 .	" " "	" " "	
0.0156 . .	" " "	" after standing.	
0.01 . . . .	" " "	" " "	
0.009 . . .	" " "	" " "	
0.008 . . .	" " "	" " "	
0.007 . . .	" " "	.....	
0.006 . . .	" " "	.....	
0.005 . . .	Positive after cooling and standing for 45 minutes.	Positive after standing.	
0.004 . . .	Positive after cooling and standing for 1 hour.	.....	
0.003 . . .	Positive after cooling and standing 1 hour 20 minutes.	.....	
0.0025 . .	Positive after cooling and standing for 1 $\frac{3}{4}$ hours.	Positive after standing.	
0.002 . . .	Negative (amorphous deposit) after standing for four hours.	.....	
0.00125 .		Positive after standing	
0.000625		Negative after standing for $\frac{1}{2}$ hour.	

*Conclusions.*—Nylander's Test is not of much value for the testing of solutions containing less than 0.5 per cent. dextrose.

Fehling's solution is the most sensitive, showing positive reaction with a solution containing only 0.00125 per cent. of dextrose.

The phenyl-hydrazine test is highly sensitive, showing positive reaction with 0.0025 per cent. dextrose solution after allowing the test to cool and stand for 1  $\frac{3}{4}$  hours.

Phenyl-hydrazine test solution possesses fairly stable keeping qualities.

The above experiments and conclusions were made in the Spring of 1907, at the suggestion of Prof. G. H. Meeker, then professor of chemistry of the Medico-Chirurgical College, Philadelphia. Pa. In 1908, Meeker and Stamm<sup>1</sup> independently duplicated these exper-

<sup>1</sup> *Bulletin of the Medico-Chirurgical College of Philadelphia*, Dept. of Pharmacy, Vol. 111, No. 3, Feb.-March, 1908, page 15.



iments and arrived at essentially the same general conclusions. The experiments and conclusions outlined in this paper are herewith offered merely as additional evidence upon the subject of the relative sensitiveness of these tests.

## A STANDARDIZATION OF DIGITALIS PREPARATIONS.<sup>1</sup>

BY EDGAR BERRY, M.Sc., A.I.C.

In presenting the following treatise I wish to thank H. E. Annett, Esq., M.D., D.P.H. (late professor of comparative pathology of Liverpool University), who has very kindly performed the injections for the Minimum Lethal Dose experiments, I myself not being licensed for this, and also Messrs. Evans Sons, Lescher and Webb, Ltd., for permission to publish results obtained in their research laboratories at Runcorn.

From my last investigation of *Digitalis Purpurea* (*P. J.*, Dec. 26, 1915), based on frog heart perfusions, three conclusions were drawn.

1. The water-soluble glucosides of digitalis apparently have the most desirable tonic and slowing effect on the heart, and are non-cumulative and non-toxic.

2. Digitoxin is cumulative and toxic, appearing to enter into actual combination with the heart muscle.

3. The leaf saponins have a harmful and toxic effect on the heart.

The constituents of digitalis vary to a very large extent under different conditions of growth. This variation is influenced by climate, soil, conditions of growth (sunshine or shade), humidity, and period of growth. For example, I found a sample of Spanish leaves to be very rich in saponin, although, apart from this, the perfusion experiments showed a good physiological action. Again, a tincture made from the first large leaves of seedlings of four months' growth from the first appearance of leaves, packed closely together in cold frames (thus excluding sunlight), I found to have the action of pure water soluble glucosides, digitoxin apparently not yet having been formed.

From these considerations—in view of the number of existing official preparations containing the whole of the soluble constituents

<sup>1</sup> Reprinted from *The Pharmaceutical Journal and Pharmacist*, July 26, 1919.

of digitalis—it is of great importance that attention should be drawn to their standardization.

Many methods have been put forward within the last few years, but none are entirely satisfactory when taken alone.

The favorite method of standardization has been by the Minimum Lethal Dose method—that is, the amount (calculated per 100 Gms. body weight) which, injected into the lymph sac of the frog, is just sufficient to kill.

Different physiologists place different time limits on this experiment—some two hours, four hours, six hours, etc. A few hours after injection the frogs become very lethargic, and it is extremely difficult to differentiate with any degree of accuracy between slight reflexes and total death. In several cases I have known frogs from which no reflex could be obtained at the end of the fourth hour, recover during the night.

Again the strength of tinctures containing excess of saponin comes out too high by this method—notably the tincture from Spanish leaves which I mentioned before—although when the drug is taken by the mouth the action is weak, digitonin (saponin) being unabsorbed in the intestine.

A sample containing a high percentage of water soluble glucosides was under strength when tested by this method, although on perfusion its action was quite powerful and desirable.

The objections to the Minimum Lethal Dose method (by injection) are:

1. A large number of frogs is required for each sample.
2. A vivisection license is necessary, and consequently the chemist cannot standardize his samples by this means.

Up to the present the best standardization put forward for digitalis preparations is Dr. Martindale's colorimetric estimation.

This method gives very concordant results with the M.L.D. values and eliminates frog variation; but, unfortunately, it does not differentiate between saponin and digitalein, and, furthermore, does not give the full digitoxin strength, some of the latter being undoubtedly precipitated along with colloidal matter on the dilution of the original tincture with water (the alcohol strength not being sufficient to hold it in solution) or is "absorbed" by the kieselghur used in filtration. As the digitoxin content does not run parallel with the digitalein in all samples (which I mentioned before), this

may give rise to inaccurate results, especially when dealing with tinctures of which the history and origin are unknown.

Some investigators claim to have standardized digitalis preparations by the use of "pithed" frogs and the Williams Apparatus, injecting the drug and noting (1) the time taken to kill the heart, and (2) the number of heart beats; calculating their results from standard tinctures of digitalis or from solutions of strophanthin. From my own tests I have not found this method reliable.

M.L.D. methods by injection show toxicity only and not therapeutic value.

#### PERFUSION EXPERIMENTS.

The apparatus used was in some respects similar to that described in my first paper (*P. J.*, Dec., 1915). I found it necessary to modify it very considerably.

The glass reservoir A contains Ringer's normal saline solution. B contains a solution of the tincture to be tested 1 per cent. in Ringer's solution.

The reservoirs were fitted with internal tubes as before (to keep the pressure constant). The stand which carried these was graduated on the upright, the zero mark being placed in such a position that the level of the lower ends of the air-tubes A and B were the same height from the table as the end of the canula C. The pressure is thus regulated by raising or lowering the cross-arm S. The Y tube, mentioned before, was substituted by a combination of three 3-way taps, which I found much more convenient than clips. The frog was "pithed" and dissected as before, a glass canula being inserted into the inferior vena cava and carefully ligatured, care being taken that no leakage was possible at the joint—the two aortæ were left intact in this experiment and the solutions perfused through the body to the other cut end of the inferior vena cava, which was left open, thus allowing the perfused solutions to escape from the body, through the perforated frog plate, into the tray T, and thence to the outlet "N," which is a glass tube of  $\frac{1}{8}$  in. bore. The drops of liquid from here operate the small trigger "K," which was counterbalanced and connected up with the writing lever "R"; thus each drop was registered on the tracing.

"S," the heart lever, is connected to the heart as before.

"F," the time marker, registers every five seconds.

The apparatus was arranged so that the height of the air-tubes



was 2 Cms. above the level of the canula "C," the solution thus being delivered at a slight pressure. The technique of the perfusion may be found on referring to my first paper. Previous to the experiment the saline content of the glass canula and tube as far as the tap "X" was accurately measured in drops for each canula, and this amount allowed for in the tracings.

It seemed feasible if the same conditions were maintained as regards (a) rate of flow of the perfusing solutions—*i.e.*, constancy of pressure from the supply reservoir—and (b) the use of solutions of equal percentage strength, that the quantity of liquid perfused through the heart should be directly proportional to the strength of the preparations used.

In this perfusion test only a certain proportion of the active constituents are used up; but we may reasonably assume that, provided the above conditions are observed, the amount absorbed by the tissues will be proportional to the weight of the hearts used; or, carrying this hypothesis still further, to the respective body weights of the frogs used (subject, of course, to slight frog variation). The amounts used, therefore, reduced to the values per 100 Gm. frog, should be directly proportional to the strengths of the solutions, and thus to the respective M.L.D.'s.

The following table of results, calculated per 100 Gm. frog weight, was obtained from various tinctures by this method. The M.L.D. of each tincture was obtained by the colorimetric estimation, and also by the actual Minimum Lethal Dose method by injection, and recorded in the table.

The time taken to kill the heart in these experiments showed no striking similarities. This discrepancy is probably due to the variation in relative quantities of the several glucosides present.

Summarizing the table, the quantity of solution necessary to kill the heart (recorded on the tracing in drops) approximates very nearly in tinctures of the same Minimum Lethal Dose, and is directly proportional in tinctures of different strengths. The values obtained, I admit, are merely measures of toxicity, but the therapeutic action can be actually seen during the experiment, and excess of any one glucoside may be easily detected in the tracing. Although these results approximate fairly well, yet I do not consider them sufficient for the standardization of a tincture by this means alone.

Considering the subject now from a chemical standpoint, the solution of the difficulty seems to lie in estimating the relative quan-

Preparation Tested.	Expt.	Number of Drops Perfused Calculated per 100 Gm. Frog.	M.L.D. from Graph.	M.L.D. Colorimetric.	M.L.D. by Injection.
Tinct. B. ....	1	1032	0.605	0.6	0.55 0.6
" .....	2	1032			
" .....	3	1031			
Tinct. 10 .....	1	649	0.5 to 0.55	0.75 much deposited since perfusion expt. was done.	No data
" .....	2	579			
Standard Tinct. 2. . .	1	1063	0.615	0.65	0.6 to 0.65
" .....	2	1064			
Tinct. 21.3.18 .....	1	640	0.43 to 0.48	0.4 to 0.5	0.4
" .....	2	540			
Tr. from Extract Dilution 1 in 10 ....	1	1008	0.6	No data	0.6
Dilution 1 in 7.5. . .	2	726	0.51	No data	0.45
Tinct. 5 .....	—	561	0.45	0.45 to 0.5	No data
Tinct. A. ....	—	517	0.43	0.4 to 0.45	No data
Standard Tinct. 1, 29.9.16 .....	—	1231	0.67	0.6 to 0.75	0.7

tities of the glucosides present. I therefore devised the following colorimetric processes.

These are partly on the lines of Dr. Martindale's method, but essential differences will be found in the extraction, precipitation, filtration, and also in the "working up" of the resulting glucosidal residues.

#### COLORIMETRIC PROCESS A: FOR WATER SOLUBLE GLUCOSIDES.

In this estimation the idea is to obtain the water soluble glucosidal content only, and to eliminate digitoxin and saponin. Alcohol is removed from the tincture to be tested and cold water solutions are used to eliminate as much digitoxin as possible, this glucoside being almost insoluble in cold water. Extraneous matter is removed by treatment with lead acetate solution, filtration being effected through kieselguhr plates in Buchner funnels. Excess of lead is removed by sodium phosphate, and the solution again filtered through kieselguhr. Precisely the same conditions must be observed in each estimation, and similar amounts of kieselguhr used.

In this way any traces of digitoxin are also eliminated by "adsorption." The solution is now evaporated on the water bath in the presence of chalk, and the residue purified by solution in methyl alcohol and chloroform and filtration. Saponin is then precipitated by the addition of ether, filtered off, and the filtrate evaporated to dryness. At the various stages aliquot parts of the solution are taken to avoid loss in filtration, and the experiment arranged so that the final residue is equivalent to 7.5 Cc. of the original tincture. The final residue is dissolved up in 3 Cc. of glacial acetic acid. .2 Cc. of this solution is then mixed with 2 Cc. of Frohde's reagent in a 4 in.  $\times$   $\frac{1}{2}$  in. test tube, allowed to stand for fifteen minutes, and the color produced compared with the color chart.

(=Values for experiment A.)

The color chart is painted from actual estimations, and requires a little explanation.

The "Equivalent Minimum Lethal Dose" values are noted separately under each color for each of the two colorimetric estimations.

The "relative strength" values denote the amount of glucosides extracted in the various colorimetric estimations, taking the color produced by the water soluble glucosides extracted from a standard tincture (M.L.D. by injection = 0.75) by process A, as unity.

#### PROCESS B: COLORIMETRIC FOR TOTAL GLUCOSIDES.

In this second estimation an alcoholic strength of 70 per cent. is maintained throughout, in order to keep all the glucosides in solution. The extraneous matter is removed by lead acetate, but is filtered off through ordinary filter paper only, *no kieselguhr* being used. The excess lead is removed by sodium phosphate, and the filtrate evaporated to dryness in the presence of chalk to prevent hydrolysis. The glucosides are dissolved out by repeated extraction with chloroform, the solutions being filtered, bulked, and evaporated to dryness. Aliquot parts of the solution are taken at the various stages as before, to avoid loss in filtration, and the experiment is arranged so that the final residue is equivalent to 7.5 Cc. of original tincture. The final residue is dissolved up in 3 Cc. glacial acetic acid. 0.2 Cc. of this solution is taken and mixed with 2 Cc. of Frohde's reagent in a 4 in.  $\times$   $\frac{1}{2}$  in. test tube as before, and, after



standing fifteen minutes, is compared with the color chart, noting the values for experiment B.

The colors produced in this process (B) are much darker than in process A. They are also more inclined to approach a reddish-brown shade. This is due to the presence of *all* the glucosides in the residue, and probably impurities, such as traces of chlorophyll.

This, however, is immaterial, as it is the "*density*" of the color which we must compare.

The correct way to match the colors is to examine the tubes by direct transmitted light, with the eyes wide open, holding a piece of white paper behind them at an angle of 45°. Then slightly close the eyes and look at the color chart.

In process B, should the value compare with tubes "d" or "e," it is too dense to be judged with accuracy on the first color chart.

A more dilute mixture must be made. This is accomplished by taking 0.1 Cc. only of the acetic glucosidal solution and introducing it into 4 Cc. of Frohde's reagent, allowing to stand for fifteen minutes, and then comparing the tubes with the second chart.

The value may thus be accurately determined, as the "relative strength" values on Chart 2 are strictly comparable with those on Chart 1, the colors having been painted directly from known tubes and the "relative strength" values worked out and checked by experiment.

The result from Process A gives *water soluble glucosides only*. This I shall call the "Therapeutic Value" of the tincture.

The result from B gives *Total Glucosides*—viz., water soluble glucosides, saponin and digitoxin. (The residue here is not very pure, but this does not greatly affect the colorimetric estimation, whereas weighing would be inaccurate.) Subtracting A from B we get the "Toxic Value" of the tincture.

We can therefore compare toxicity by means of the ratio

$$\frac{B-A}{A} \text{ i.e., } \frac{\text{Toxic Value}}{\text{Therapeutic Value}}.$$

If we estimate this for a standard tincture and for an unknown tincture, and compare the two (using "relative strength" values) we can compare the toxicity of the samples, as in the following example:—

	Standard Tincture.	Tincture 213.18.
Therapeutic value (A)....	1	1.5
(W. S. Glucosides) .....		
Total Glucosides .....	2.5	4.0
Value B .....		
Toxic Value (B-A).....	1.5	2.5
Ratio $\frac{B-A}{A} =$	$\frac{1.5}{1} = 1.5$	$= \frac{2.5}{1.5} = 1.66$

thus showing that the Tincture (213.18) is relatively more toxic and therefore not so beneficial as the Standard Tincture.

A desirable standardization of any tincture would be as follows:  
(1) Conduct two colorimetric estimations by process A and B. Note the M.L.D. value, and the therapeutic value (A). Then check the M.L.D. value from experiment B, and work out the ratio  $\frac{B-A}{A}$ . An increased M.L.D. value from (B) denotes excess toxicity, which would be confirmed by the ratio  $\frac{B-A}{A}$ . The excess toxicity may be due to either saponin or digitoxin (although for oral medication the presence of saponin is of little import, as I mentioned earlier).

(2) Carry out the perfusion experiment, using male frogs and the tincture 1 per cent. in Ringer's solution, continuing the perfusion until the heart stops. Then calculate the number of drops required for 100 Gm. frog, and find the result on the M.L.D. graph. Notice the time taken to kill the heart, as this gives some guide as to the relative quantities of the several glucosides present—*e.g.*, a long tracing with, say, 0.5 to 0.6 M.L.D. would indicate a high water soluble glucosidal value and a corresponding low digitoxin value and *vice versa*. The tracing would also show the therapeutic action; any abnormal variation in the composition of the tincture being easily detected. (This was explained at length in the treatise which I summarized previously.)

A second "two or three minutes" perfusion on another frog, reperfusing Ringer's solution again to recovery, would give us useful information as regards therapeutic activity. The M.L.D. values obtained from the graph could be checked by injection if desired by using four frogs only, the doses given being

- (1) Slightly *below* the calculated M.L.D.
- (2) and (3) M.L.D. *as calculated*.
- (4) Slightly *above* the calculated M.L.D.

No. 1 frog should live. Nos. 2 and 3 frogs should be questionable. No. 4 frog should die.

I do not consider these injection experiments necessary, and consequently no license would be required for carrying out the standardization.

From the foregoing experiments it is now easy to judge whether a tincture is desirable or not, and to estimate accurately its strength. After adjusting the tincture it should be rechecked.

In conclusion, too much stress cannot be laid on the methods of cultivation of the drug. The best strains of plants (tested by experiment) should be used, and the gathering of the leaves done under strict supervision. These items should be carried out year by year under as nearly the same conditions as possible, if uniform tinctures are to be obtained.

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## IODINE TINCTURES, WATER SOLUBLE.<sup>1</sup>

BY TORALD SOLLMAN, M.D.,

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Proprietary preparations of iodine have been on the market for many years and advertised to physicians as superior to the official preparations—tincture of iodine and Lugol's solution (*Liquor Iodi Comp.*, U. S. P.). The superiority claimed for these proprietary preparations is based on the allegation that the potassium iodide in the official preparations causes a local irritant action which is avoided in the proprietary preparations. The allegations seem improbable—certainly the local irritant action of potassium iodide must be regarded as negligible, as compared with that of hydriodic acid contained in the proprietary preparations. Rather, it was surmised that any difference in local irritation following the use of the proprietary preparations was due to the fact that the iodine content in these preparations was insufficient to produce the irritation or, on the other hand, sufficient to have only a slight, if any, therapeutic effect.

<sup>1</sup> From the Department of Pharmacology of the Western Reserve University School of Medicine. Reprinted from the *Jour. Amer. Med. Assoc.*, Sept. 20, 1919. This investigation was supported by a grant from the Therapeutic Research Committee of the Council on Pharmacy and Chemistry of the American Medical Association.



The manufacturers do not seem to have published, and presumably do not possess, any comparative data on the degree of irritation produced by their preparations, as compared with the official tincture of iodine after this has been diluted so as to reduce its iodine content to that of the proprietary preparations. It was therefore decided to determine this point by applying various iodine preparations of an equal iodine content to the skin and also by extending the experiments in other directions. In these experiments two widely advertised proprietary preparations—Burnham's Soluble Iodine<sup>2</sup> and Sharpe and Dohme's Surgodine<sup>3</sup>—were included.

Since these, however, are more or less secret in composition, I have devised a non-secret preparation of the same character by the use of hydrogen iodide (hydriodic acid). The details of this preparation will be published in a pharmaceutical journal. Before use, each of these preparations was reduced by the addition of alcohol to a free content of 2.2 per cent. (2.2 Gm. in 100 Cc.).

COMPOSITION OF IODINE PREPARATIONS USED.<sup>4</sup>

Nature of Preparation,	Free Iodine.	Percentage of Combined Iodine (Including HI).	Acidity as of HI.
Alcoholic solution. . . . .	2.2	0.4	0.2
U. S. P. tincture (KI). . . . .	2.2	1.6	0.07
Alcohol with HI (author's formula) . . . . .	2.2	0.7	0.6
Burnham's Soluble Iodine . . . . .	2.2	2.7	1.4
Surgodine . . . . .	2.2	1.2	0.8

The accompanying table shows the composition of the solutions used, the total iodine being the same, the principal difference being in the acidity, which ranges from a minimum of 0.07 per cent. in the U. S. P. tincture (containing potassium iodide) to a maximum

<sup>2</sup> Examination in the A. M. A. Chemical Laboratory indicated Burnham's Soluble Iodine to be a solution of iodine in alcohol made miscible with water by the presence of some iodide and containing approximately 3 Gm. of free iodine and 2 Gm. of combined iodine in approximately 100 Cc. (*J. A. M. A.*, 50: 1055 (March 28), 1908).

<sup>3</sup> The A. M. A. Chemical Laboratory reported that Surgodine was an alcoholic liquid containing 2.51 Gm. of free iodine and 1.78 Gm. of combined iodine, probably present chiefly as hydrogen iodide, in 100 Cc. (*J. A. M. A.*, 70: 257 (Jan. 26) 1918).

<sup>4</sup> The numbers represent grams per hundred Cc. of preparation. Before use, each preparation was reduced with alcohol to a content of 2.2 per cent. of free iodine.

of 1.4 per cent. in Surgodine. The special preparation which I devised is intermediate and contains 0.6 per cent. The total combined iodine (including potassium iodide or hydrogen iodide) ranges from 0.4 per cent. in the alcohol solution to 2.7 per cent. in the Burnham preparation.

*Effects on the Skin.*—The solutions were painted on the skin of the inner surface of the forearm, each solution covering an area of from 15 to 20 Mm. diameter; each application was allowed to dry before the next was added.

The results did not show any significant or constant differences. The actual results indicated that Burnham's preparation was the more irritant, and the U. S. P. tincture (reduced to the same iodine percentage) was the less irritant, but the differences were so small that they could easily be accidental.

In a preliminary test with three applications, no material difference could be detected between the different solutions.

In a second series, a measured quantity of solution was applied to two spots in three courses. The first course consisted of five applications at intervals of five minutes, and then a pause of thirty-five minutes. At the end of this time, the skin of all the areas was slightly tender. The second course consisted of five applications during sixteen minutes, and then a fifty-five minute interval. There was now considerable tenderness, alike for all the areas. The third course comprised five applications during fifteen minutes. Forty minutes after the last application, all the areas were equally sore. The depth of the stains ran in decreasing order from Burnham's (most) through Surgodine, hydrogen iodide, U. S. P. tincture, and alcoholic (least); but the differences were not great.

After removing the excess of iodine with alcohol, the reddening and edema at this time appeared as follows: Burnham's most, distinct papular edema and reddening; then the alcoholic; then the others, which were about alike.

On the following morning, the order of irritation was as follows: most, both Burnham's areas; next, one of the alcoholic areas; next one of the hydrogen iodide areas; next, Surgodine; least, U. S. P.

*Precipitation of Albumin.*—Irritation is often due to precipitation of proteins, and this probably applies to the irritant action of iodine. Therefore an investigation was made to determine whether

there exist significant differences in this respect between the several iodine preparations.

Each of the diluted iodine preparations (2.2 per cent. iodine) was diluted with 10 volumes of water, to avoid precipitation of protein by the alcohol, and the diluted solution added to an equal volume of a 10 per cent. solution of natural egg-white in physiologic sodium chloride solution.

The simple tincture, that with hydrogen iodide, Burnham's preparation, and Surgodine, produced an apparently identical coagulum. The U. S. P. tincture (diluted in the same way) produced only a turbidity; this also when the quantity of the iodine solution was doubled. Next morning, the albumin was coagulated as with the others. The reaction to litmus remained neutral.

The restraining action of the potassium iodide is limited, for the addition of an equal quantity of the potassium iodide tincture to the hydriodic acid tincture does not prevent immediate coagulation (1 volume potassium iodide tincture, 1 volume hydrogen iodide tincture, 10 volumes of water).

It is evident, therefore, that the potassium iodide of the official tincture has a restraining effect on the coagulation of protein. This would tend to make it less irritant than the other preparations. It is conceivable that this may be disadvantageous in skin protection, in which the fixative action is probably desirable. In this case, however, there is no object in using a water-miscible preparation, and the simple alcoholic solution of iodine would be fully as good as any of the others.

*Capillarity and Spreading.*—Dilute tinctures of iodine, when placed on the skin or on parchment, tend to distribute themselves so that the solution becomes most concentrated at the periphery (as in the accompanying illustration). In this manner, the periphery of an application on the skin may be blistered when the center is scarcely affected. If this property were more marked in one specimen than another, this would be equivalent to greater irritation. The illustration shows that this uneven distribution runs in the order: U. S. P. (potassium iodide tincture), most; Burnham's soluble iodine; hydrogen iodide tincture; Surgodine; alcoholic tincture (containing no potassium iodide), least.

The differences are in favor of the simple alcoholic tincture (which was formerly official) and adverse to the tincture containing potassium iodide (which is now official); but they do not im-



press me as of great importance, since they are even less marked on the skin.

I tried also to demonstrate differences in capillarity by the spreading or rise through filter paper; but the variations were insignificant.

*Conclusions.*—The presence of potassium iodide in the official tincture of iodine does not seem to render this preparation more irritant. On the contrary, it is somewhat less irritant to the skin, and much less precipitant to proteins, than the simple alcoholic tincture, or the secret and non-secret “miscible tinctures.” The more even spreading and the more rapid coagulation of protein render the simple alcoholic solution of iodine probably the best for the “disinfection” of the skin; while the delayed protein precipitation by the U. S. P. tincture would probably render this somewhat superior for the disinfection of open wounds. The secret and non-secret “water-soluble tinctures” do not appear to have any material advantages.

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## PURIFIED ETHER AND THE VARIATIONS IN COMMERCIAL SAMPLES.<sup>1</sup>

BY A. J. JONES, PH.C.

To bring before the notice of the Conference such a subject as ether almost requires apology, for it is one that has received a good deal of attention in the past, and little can remain to be said about it that is really new. But, after making some comparisons between commercial brands, it was thought there were one or two points of interest that would bear consideration, and upon which attention would not be wasted. As everyone knows, there is “ether” and “purified ether”; the former being for the ordinary requirements of medicine and pharmaceutical practice, while the latter is usually taken as having been specially defined for employment as an anesthetic. Purified ether, however, finds other uses, and in some branches of manufacture it is necessary to be very strict in limiting traces of impurities; but it is not so much the object of this paper to enter into that part of the question as it is to draw attention to certain differences existing between what is called by the makers

<sup>1</sup> Reprinted from *The Pharmaceutical Journal and Pharmacist*, July 26, 1919.

“anesthetic ether” and the definition of the “purified ether” of the Pharmacopœia. The results of the examination of nine samples of “Ether Purificatus” prepared by different manufacturers is set out below for illustration. The Pharmacopœia does not demand that ether shall be made according to any particular recipe, but it defines the *character* of the ether, by prescribing a definite specific gravity and a limited boiling point range, and then makes special requirements as to *impurities*, leaving little doubt as to the intention of providing a fairly pure ethyl oxide.

#### THE CHARACTER OF THE ETHER.

A glance at the table will show seven samples from industrial methylated spirit, and two from rectified. The latter, as one would expect, are B.P. in character, but of the seven methylated ethers only two answer this description, and the deviations afford interesting comparison. Now it is difficult to believe that, with differences of this sort, identical results are to be obtained from the administration of the different ethers, and since employment as an anesthetic is the use, perhaps, to which importance attaches most of all, this question of uniformity of product and effect is one deserving some consideration.

One is sometimes met by the statements from different surgeons that it is only particular brands of ether that give them satisfactory results, and others again will only use ether prepared from rectified spirit; while a case occurred only a short time ago where an officer connected with an American military hospital, expressed himself as being so dissatisfied with English ether that he gave up using it, and imported all his further supplies for that hospital from America. One is apt to attribute this sort of thing simply to prejudice, but it by no means follows that that is the proper view to take, and I believe it is not very far from the truth to say that during the war a special demand was made for B.P. ether, and that special facilities were given by the authorities for its conditional production. In this connection there is a particularly interesting report by Dr. Cotton of the McGill University, Montreal, on his observations concerning the physiological effects of ether and their causes. His opinions are rather startling, but as they appear to have been demonstrated and to have received certain acceptances they may be briefly stated. Shortly put, he considers that absolutely pure ethylic ether is not

anesthetic in the full sense of the term; that it is narcotic, but not analgesic, and that it is to traces of certain "impurities" formed in the manufacture of the ether to which the proper anesthetic effects are due; suggesting ethylene as being the analgesic substance. In furtherance of this view, some remarkable demonstrations were given of the combined effect of ether and ethylene, but beyond mere mention of this I must refer those interested in the matter to the original communication.<sup>2</sup> The point that it is desired to emphasize in these notes is: Is there any real difference between the action of these low boiling mixed ethers and the higher boiling official article, and is there any valid reason for the preferment of the one to the exclusion of the other from the Pharmacopœia? The difficulty is that one cannot but suppose there were definite reasons for making the restrictions of the Pharmacopœia, yet there remains the indisputable fact that very large quantities of unofficial "anesthetic ether" are requisitioned (even, perhaps, larger quantities of this than of the literally official article) and apparently used with success. If there is no practical difference, then it is very desirable that the official requirements should be modified so as to include both types; but if an undoubted difference is observable, then it is still more desirable that the two types should have recognition, so that all ambiguity might be removed and a distinction drawn as to the special adaptations of the particular ether. This question is one the solution of which is medical rather than pharmaceutical, for it is to do with observed physiological effect; but it is certainly very desirable for the pharmacist to know exactly where he stands when he is called upon to handle material ostensibly the same, but virtually different, which is used without recognition of probable differences in properties.

Closely connected with this is the demand for "absence of methyl compounds" from purified ether. One might, perhaps, be allowed to express the opinion here that it would be a great advantage in cases of this sort where mere traces are being dealt with, if something rather more specific than bare *absence* of a *class* of compounds was required. This is all very well where the desire is simply to maintain a standard of commercial purity, but it is an entirely different thing when tests are introduced having behind them the idea of physiological effect. Such tests should be very distinctly noted and treated in as fully an explanatory a manner as possible. For

<sup>2</sup> *Journ. Canad. Med. Soc.*, Sept., 1917; *Med. Rec.*, Mar. 16, 1918.



purity alone can safely be left to the discretion of the pharmacist whenever discretion becomes necessary, but he is not at liberty to exercise this function in requirements which are specifically medical. Absence of direction of this sort occasionally leads to vexatious proceedings; at times it retards output; at others, through ignorance in giving but secondary consideration to a matter which may really be of primary importance, a very unsatisfactory position of affairs may be brought about.

#### THE IMPURITIES.

The Pharmacopœia prescribes tests to limit the quantity of peroxide, aldehyde, vinyl alcohol, and methyl compounds, and the usual supplies of purified ether behave with general satisfaction in these respects. One or two remarks, however, may be permissible. The test for methyl compounds would be more correctly described as a test for the presence of methyl alcohol and such substances as break down to formaldehyde under the influence of the oxidation. Complaints have been made that the test is erratic in its indication, and it is believed the test was not inserted in the Pharmacopœia with the unanimous approval of manufacturers. Faults of sensitiveness have been mentioned (Dott, *P. J.*, 17/3/17, p. 236) and ascribed both to the fuchsin and to the method of preparing the reagent. Different samples of fuchsin do undoubtedly vary, but I have been fortunate in having samples that never failed to detect so small a quantity as 1 Mgm. of methyl alcohol in 5 Cc. Experience has shown, however, that a Schiff's reagent which may be very sensitive when freshly made is preferably not used after six weeks' keeping; at three months it is useless for the purposes of this test. It has been pointed out (Dott, *C. and D.*, 20/2/15, p. 52) that highly purified methylated ether and ether from rectified spirit will give positive reactions, and this can readily be confirmed. It appears to be due to traces of compounds occurring in the ether, quite apart from its origin, but rectified ethers seem to give a fairly constant indication of about an apparent 0.02 per cent. of methyl alcohol. Some methylated ethers approach this very closely, although on the whole they are distinctly higher. That the impurities responding to this test are not the same in each specimen of ether is seen by the different behavior after extraction, first with alcohol and then followed by water. Some ether was taken and washed with

5 Cc. of 10 per cent. alcohol, which was separated. Two further washings were rejected, but the fourth reserved. It was then further washed with two lots of 5 Cc. of water, the second lot being reserved for the test. The results are shown in the table, quantities being Cc. methyl alcohol.

Sample.	10 % Alcoholic Extract.		Aqueous Extract.
	1 st	4th	2d
Rectified .....	.001	.0002 (say)	nil
Meth. (boiling point) .....	.0015	Very faintly blue nil	nil
Meth. (low boiling point) .....	.0015	.0006 (say)	.002
Meth. (low boiling point) .....	.0025	.0004 (say)	.001

And if two portions of the same sample of ether be extracted, one with 10 per cent. alcohol and the other with water only, and the test applied, the difference between the two results varies with different makes of ether—the aqueous extract from one ether may give twice as strong an indication as the alcoholic extract, while with another ether it may be six or even more times as great. Of course, the effect in aqueous solution is not to be compared with that in the 10 per cent. alcohol, on account of the increased oxidizing power of the permanganate where the alcohol is absent.

But the experiment shows that while with some samples there are impurities extractable by alcohol, leaving no other oxidizable bodies behind, yet with others we may have the same impurities and further traces of other oxidizable substances as well. In short, the impurities vary with different ethers.

Rather than attempting any method of overcoming the inherent “ether effect” in this test, and bearing in mind the possibility of variation in its behavior in different hands, it is suggested that comparison against a given standard is much better than demanding a negative reaction. Such a procedure not only has the obvious advantage of being definite, but also ensures the proper working of the test, and gives evidence at once if the reagents are insufficiently sensitive. Probably a limit of an apparent 0.05 per cent. of methyl alcohol would be quite fair for a modern purified ether from methylated spirit. As to other impurities, since they are not specially guarded against in the Pharmacopœia, one may assume that such as occur in the usual course of events are not considered objectionable from the medical point of view. But the finding of the trace of formaldehyde in a sample of rectified ether which had been in stock

somewhat over a year, emphasizes very clearly the absolute necessity of the proper storage of ether and the desirability of not holding stocks too long. On one occasion, however, when requiring a very pure ether for some manufacturing purpose, it was thought desirable to estimate the amount of acetone or ketone present. The results are given in the table, and speak for themselves. Acetone is of fairly constant occurrence in methylated ethers, but one or two makers produce an ether of such purity as to give an all but negative reaction with the nitroprusside test. For the determination an adaptation of Scott-Wilson's method was employed, and, for the purpose of comparison, was quite satisfactory, although not exactly precise as here used. But I believe, by a little further development, it is capable of consistent accuracy when applied to ether.

#### EXPERIMENTAL.

*The distillation* was made with 100 Cc. of the ether in a three-bulbed Ladenburg flask connected with a small worm condenser, and using a standardized thermometer. A few pieces of pumice were placed in the flask. The correction for temperature was about 0.05 of a degree, and was, therefore, negligible. The source of heat was a small water bath, the cover having a hole cut in the center so as to expose only a small section of the bottom of the flask. *Methyl Compounds Test.*—A slight modification of the B.P. procedure is adopted for this test. The Schiff's reagent is prepared by powdering 0.5 Gm. of fuchsin and digesting with 90 Cc. of sulphurous acid (B.P.) overnight, by when it should be decolorized, then adding water up to 250 Cc. and filtering. For the test 5 Cc. of the ether is shaken up with 5 Cc. of a 10 per cent. mixture of absolute alcohol with water, and, after separating, drawn off into a boiling-tube.

For comparisons a dilution of 1 Cc. of pure methyl alcohol in 500 Cc. of water is made, so that each half of a Cc. represents 0.001 Cc. of methyl alcohol. A series of three test-tubes, similar to the above, are taken, and 0.5, 1.0, and 1.5 Cc. of the dilution run in, followed by  $\frac{1}{2}$  Cc. of absolute alcohol, and then  $4\frac{1}{2}$ , 4, and  $3\frac{1}{2}$  Cc. of water added respectively, to make a total of  $5\frac{1}{2}$  Cc., which is approximately the volume of the ether extraction. The B.P. test is now followed, but, after adding the 5 Cc. of Schiff, each tube is thoroughly stirred with a thermometer, and carefully brought to a temperature between  $45^{\circ}$  and  $50^{\circ}$  C. The test is then set aside



until it has gained room temperature, or, preferably, for an hour. Under these conditions the test has given very satisfactory results. The reason for adopting this procedure was the experience that, with a *freshly-made* and *sensitive* Schiff, a bluish violet coloration was always obtained that was very confusing, no doubt due to acetaldehyde, and which would vary from time to time. But it was noticed that by heating as suggested this color would suddenly disappear at about 45°, and then the color due to the formaldehyde asserts itself. With 0.001 Cc. of methyl alcohol it requires about a quarter of an hour, but with 0.003 Cc. the color asserts itself almost as soon as the last trace of the fallacious coloration has disappeared. As thus set out the test makes comparison of an "apparent" 0.02, 0.04, and 0.06 per cent. of methyl alcohol in the 5 Cc. of ether.

One cannot urge too strongly the desirability of running the controls every time a test is made. There are too many variables influencing the test for one to rely solely on judgment of coloration.

*Alkaline Silver.*—A little 2 per cent. silver nitrate is added to an equal volume of caustic soda solution (20 per cent.) and cleared by the addition of just sufficient ammonia. Very pure ethers when shaken with this—say about 5 Cc. with 3 Cc. of reagent—give very little reduction indeed; on setting aside for five to ten minutes some samples are all but negative in reaction.

*Formaldehyde* may be detected by the usual gallic acid ring test.

*Acetone.*—This may be detected qualitatively by applying Rothera's modification of the nitroprusside reaction as described by Finnemore (*P. J.*, 25/7/14, pp. 139 and 160). Scott-Wilson's method<sup>3</sup> consists in precipitating the acetone or ketone as the mercury compound  $\text{HgC}_3\text{O}$  ( $\text{HgCN}$ )<sub>4</sub> by reacting with an alkaline silver-mercury cyanide solution and determining the mercury in the precipitate. It is an exceptionally delicate reaction, and one must always be careful to have an *excess* of reagent. In making qualitative tests nothing is easier than to achieve a negative indication through taking too much acetone. Alcohol does not appear to have any influence in small quantity, but aldehyde reacts after the manner of acetone, and ammonia, if present would also interfere. The reagent is prepared by dissolving 5 Gm. of mercuric cyanide and 90 Gm. of caustic soda in 600 Cc. of water, then 1.5 Gm. of silver nitrate in 200 Cc. of water, and gradually pouring this solution into the former under constant stirring. The reagent is then set aside to

<sup>3</sup> *Journ. Physiol.*, 1911, Vol. 42, 444.

deposit and become a brilliant solution. An acid mixture consisting of 40 Cc. nitric acid, 5 Cc. sulphuric acid, and 55 Cc. of water is required for dissolving the precipitate, and a standard solution of sulphocyanide, of which 1 Cc. will be equivalent to 1 Mgm. of mercury (about 1 Gm. KSCN per liter). The adaptation used is as follows:—1.08 Gm. of mercuric oxide is taken, mixed with a little water, dissolved by the aid of nitric acid, and then diluted to a liter—1 Cc. is equivalent to 1 Mgm. Hg. Twenty-five Cc. of this solution are mixed with 15 Cc. of the “acid mixture” and 2 Cc. of a saturated solution of iron alum, and then titrated with the sulphocyanide solution; a reddish-brown tint marking the end point. The value of the sulphocyanide in terms of mercury is thus obtained by a simple calculation. It is to be remembered that the presence of chlorides would vitiate this reaction.

In testing rectified ether 8 Cc. may be taken, but with methylated only 4 Cc., and with ordinary 720 methylated (not purified) 2 Cc. is sufficient. About 75 Cc. of distilled water is taken in a 100 Cc. graduated flask, and 10 Cc. of 2 per cent. silver nitrate solution, the ether is added, and the whole shaken till it is dissolved; 2 Cc. of 20 per cent. caustic soda solution are now run in, and the volume adjusted to 100 Cc. The flask is stoppered, inverted once or twice, and set aside for a minute or two; it is then vigorously shaken continuously for three minutes and then filtered. This treatment removes the aldehyde. The shaking is very necessary as otherwise traces of silver remain in colloidal suspension. Fifty Cc. of the reagent are placed in a conical flask, and then 75, 50 or 25 Cc. of the ether filtrate added according to the supposed contamination, but having rather *less than* 2 Mgm. of acetone to the 50 Cc. of reagent. The contents of the flask are thoroughly mixed, and a strong white turbidity appears within a second or two if any quantity of ketone is present. The flask is set aside over night, and in the morning the clear supernatant liquid carefully poured off under suction through a Gooch crucible which carries a moderately thick mat of pulped filter paper. (Whatman's 41 answers very effectively.) The precipitate is then washed on to the filter, and thoroughly cleansed with water till free from alkali. The filter mat and precipitate are then transferred to the original flask, disintegrated in a few Cc. of water, and then treated with 15 Cc. of the acid mixture and 2 or 3 Cc. of  $\frac{N}{10}$  permanganate to help in the oxidation. The flask is either set on the steam bath for a quarter of an hour, or boiled for one or two min-

TABLE OF ANALYTICAL RESULTS.

Distillation Temperature, 100 Cc. Taken.	Samples from Industrial Spirit, Quantities in Cubic Centimeters.							Samples from Rectified Spirit.		
	1.	2.	3.	4.	5.	6.	7.	8.	9.	10.
°C.										
Below 29°	10	—	—	—	—	—	—	—	—	—
29-30	13	—	—	—	—	—	—	—	—	—
30-31	14	20	—	—	—	—	—	—	—	—
31-32	14	15	15	—	—	—	—	—	—	—
32-33	14	16½	22	—	—	—	—	—	—	—
33-34	17	17	25	28	—	—	95	1	1	—
34-35 } B.P. {	14	18½	27	68½	97	97	2	69	94	—
35-36 } limit. {	—	8	7	—	—	—	—	21	1	—
36 and over	—	—	—	—	—	—	—	5	—	—
Recovery	96	95	96	96½	97	97	95	96	96	—
Methyl compds as "appar- ent" CH <sub>3</sub> OH per cent...	0.03	0.05	0.05	0.05	0.03	0.06	Less than 0.02	Less than 0.02	0.08 <sup>4</sup>	Less than 0.02
Pot. iodide test	Colorless	Straw	Just seen	Straw	Colorless	Colorless	Colorless	Strong lemon	Colorless	—
Caustic potash	In all samples a negative reaction									
Specific grav.	.7195	.7187	.7182	.7202	.7200	.7203	.7211	.720	.7207	.720
Tests other than B.P.										
Alkaline—silver	Black cloud, but transparent	Very slight	Nil.	Black, nearly opaque	Very slight	Slight	Slight	Very strong reduction	Negligible	—
Formaldehyde	Suspicious	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.	Distinct reaction	Nil.	Nil.
Nitroprusside test (acetone)	3 min.	Nil.	5 min.	1 min.	1 min.	3 min.	½ min.	Nil.	Nil.	—
Ketone calculated as aceto- tone in parts per 10,000.	1.8	—	0.8	5.0	4.4	3.1	7.5	0.43	0.18	0.09
(A sample of ordinary 720 "Industrial" ether showed 23.8 parts.)										

Sample 8 had been in stock for over a year.

<sup>4</sup> The methyl reaction could not be explained. This was a small sample specially obtained. These two rectified samples are given because of the abnormalities, formaldehyde and methyl compounds. In the nitroprusside test the time is that required for an unmistakable coloration to occur after adding the amount and well shaking up.



utes over a flame, to decompose and dissolve the precipitate. Care must be taken to see that the whole is taken up; with the larger quantities particles sometimes remain persistently insoluble unless rubbed down with a glass rod. The solution becomes colorless, and, after cooling, is titrated with the sulphocyanide as already described, using the iron alum as indicator. A deduction of 0.1 to 0.2 Cc. may be made for the amount required to give a satisfactory end point, but each experimenter should determine this for himself.

Each milligram of mercury represents 0.058 Mgm. of acetone. The following trials were made. A dilute acetone solution was prepared and its apparent strength determined by taking 10 Cc. together with 40 Cc. of water, and 50 Cc. of the reagent.

Determinations were then made by taking 4 Cc. of an ether and different quantities of the acetone solution, and proceeding as described above for the ether test. After making the necessary deduction for the "blank" of the ethers, the results were as follows:

Acetone Taken. Milligrams.	Acetone Found, Milligrams.	Deviation.
0.46	0.516	+ 11%
0.874	0.893	+ 2%
0.92	0.986	+ 7%
1.84	1.91	+ 4%
2.76	2.65	- 4%

Fifty Cc. each of reagent and filtrate being used. It will be noticed, consequently, that in the last test the reagent is insufficiently in excess for the quantity taken. These results were considered good enough for the comparisons desired, and the estimations were proceeded with. But it is believed that for absolute accuracy it would be necessary to keep to a fixed ratio of reagent to solution, and prepare a scale for different acetone concentrations.

This work was done in the Liverpool Laboratory of Messrs. Evans Sons, Lescher and Webb, Limited.

SOME PROPERTIES OF THE FAT-SOLUBLE VITAMIN  
(FAT-SOLUBLE A).<sup>1</sup>

The day has passed when even the most skeptical critic of novel hypotheses can deny that certain natural fats, notably milk fat, egg-yolk fat and various tissue oils, exhibit a peculiar potency in nutrition that is not shared by many other wholesome fats which enter into the dietary. Whether the property referred to be designated as a vitamin, a food accessory substance, a food hormone or auximone is of secondary interest so long as its chemical nature and mode of action are still so obscure. The fundamental fact that has been firmly established: When a suitable source of the fat-soluble vitamin as it exists either in animal fats or in green plants is lacking in the diet, nutritive disaster is certain to follow sooner or later, even when all other components of the ration are ideally adequate. We are here dealing with some as yet unidentified food factor indispensable for nutritive well-being, even though the quantity that is required may be measured with small units.

The earlier studies of the fat-soluble vitamin were largely directed to the search for its sources, so that it is now possible to catalogue a considerable list of foods of known potency with respect to the factor under discussion. The practical significance of this will be clearer to the medical practitioner when the bearing of a deficiency of fat-soluble vitamin on the genesis of certain symptoms of malnutrition is further elucidated. A shortage of the vitamin in the human dietary has already been convincingly related to the appearance of eye disease (xerophthalmia) in children; and English investigators are inclined to ascribe rickets to a similar deficiency factor. During the enforced food shortage of war-time days, the lack of butter, eggs and meats caused considerable concern to the food authorities. We have already pointed out that butter substitutes which are made from beef fats or oleo oils may be physiologically comparable to some extent with butter in their growth-promoting power, whereas those prepared from vegetable oils are inadequate in this respect.<sup>2</sup>

<sup>1</sup> From *Jour. Amer. Med. Assoc.*, Oct. 4, 1919.

<sup>2</sup> Osborne, T. B., and Mendel, L. B.: *J. Biol. Chem.*, 20: 379 (March), 1915. Drummond, J. C., and Halliburton, W. D.: *J. Physiol.*, 51: 235 (Sept.), 1917. Steenbock, H., Kent, H. E., and Boutwell, P. W.: *J. Biol. Chem.*, 35: 517 (Sept.), 1918. "A Problem Concerning Edible Fats," editorial *J. A. M. A.*, 69: 1876 (Dec.), 1917.

As might be expected, these pioneer studies of distribution are being followed by investigations of the properties of the unique something known as fat-soluble vitamin. It has not been identified with any of the recognized components of fats, such as glycerol, fatty acids, cholesterol, phosphatids or lipochromes. Several investigators, of whom the latest is Drummond<sup>3</sup> of the Cancer Hospital in London, have called attention to the ready destruction of the fat-soluble accessory food factor (*A*) after relatively short exposure to a temperature of 100° C. (212° F.). Longer exposures at lower temperatures, for example, 37° C. (98.6° F.) may be equally detrimental. This destruction is apparently not a result of oxidation or hydrolysis. The facts just cited render it impossible at the present state of knowledge to "harden" liquid oils, as is now so commonly done in the industries, without effecting a loss of the fat-soluble vitamin which the original fats may contain. This explains, further, why it is that the popular commercial hardened oils are devoid of the vitamin, whatever their origin may have been.

The specific rôle of the fat-soluble vitamin within the organism still remains unknown. The fact that it is found in certain fat depots of the body has suggested that it may play a part in the utilization of fats. Recent observations by Drummond<sup>4</sup> indicate that this is not the case, however. A deficiency of fat-soluble *A* in the diet does not exert any direct influence on the absorption of fat; and animals are able to absorb large amounts of fatty acids and presumably synthesize these into fats, in the absence of the fat-soluble vitamin.<sup>5</sup> Drummond<sup>3</sup> ventures to suggest that the latter is not a clearly defined chemical substance, but rather a "labile substance perhaps possessing characteristics resembling those of an enzyme." We shall await further investigations without the bias of a fixed hypothesis.

<sup>3</sup> Drummond, J. C.: "Researches on the Fat-Soluble Accessory Substance, I, Observations on Its Nature and Properties," *Biochem. J.*, 13: 8 (May), 1919.

<sup>4</sup> Drummond, J. C.: "Researches on the Fat-Soluble Accessory Substance, II, Observations on Its Rôle in Nutrition and Influence on Fat Metabolism," *Biochem. J.*, 13: 95 (May), 1919.

<sup>5</sup> "Fatty Acids as Foods," editorial *J. A. M. A.*, 73: 608 (Aug. 23), 1919.



NOTE ON THE QUANTITATIVE B.P. TEST FOR SODIUM SALICYLATE.<sup>1</sup>

BY J. B. P. HARRISON, F.I.C., AND F. E. CARTER, B.Sc.

The monograph of the British Pharmacopœia states that sodium salicylate must contain 99.5 per cent. of the pure salt.

The quantitative test, as given in the paragraph headed "Characters and Tests," is thus described: "2 Gms. heated to redness till gases cease to be evolved leave an alkaline residue which, when treated with water, filtered, and well washed, yields a clear solution requiring for neutralization not less than 24.8 milliliters of N/2 solution of sulphuric acid." This is practically the same test as that prescribed for quantitatively determining sodium and potassium tartrate, but whereas in this instance very accurate results can be obtained, in the case of sodium salicylate varying results are given by different experiments on the same sample.

F. H. Alcock,<sup>2</sup> in a paper entitled "Sodium Salicylate," has drawn attention to this anomaly, and attributed the unsatisfactory results obtained by titrating the alkaline solution after treating sodium salicylate in the manner above described to the retention of part of the alkali by the carbonaceous matter which is filtered off, even after this has undergone very considerable washing with distilled water. This fact we can fully confirm, and at the end of this note shall give results in confirmation. Alcock, however, did not concern himself with improving the details of the method, but put forward a new process based on the decomposition of sodium salicylate by ammonium chloride when the two are heated together in strong aqueous solution.

One of the disadvantages of the alkalimetric process as described in the B. P. is that the solution obtained for titration with standard acid is often deeply colored with carbonaceous matter, so that it is difficult to see the change in color of the indicator at the end of the reaction. This tendency to produce a solution of colloidal carbon can be obviated in two ways. Firstly, by prolonged ignition of the carbonized mass whereby the carbon is either burned away or rendered in a form denser than that of colloidal carbon. In thus heating, however, there is a danger of raising the temperature of the

<sup>1</sup> Reprinted from *The Pharm. Jour. and Pharmacist*, Sept. 13, 1919.

<sup>2</sup> *P. J.*, Fourth Series, Vol. 23, p. 597.

mass higher than that at which the alkali melts, and so losing small traces by volatilization. Secondly, by neutralizing the alkaline solution with acid, the colloidal carbon is precipitated so that, on filtering, a clear water-white solution is obtained. This is the method proposed by Warington<sup>3</sup> in his classic papers on the analysis of commercial compounds of citric acid and tartaric acid, and with slight modifications is the official method for the assay of alkali salts of organic acids of the Ninth Decennial Revision of the United States Pharmacopœia, from which the following extract is taken: "After allowing the carbonized mass to cool, disintegrate it with the aid of a stout glass rod and transfer the mass and crucible to a beaker. Add 50 Mils. distilled water and 50 Mils. N/2 H<sub>2</sub>SO<sub>4</sub>, cover the beaker with a clock glass and boil for 30 minutes. Then filter the solution and wash the residue until the washings cease to redden litmus paper. Now determine the residual acid in the cooled filtrate by titration with N/2 KHO, using methyl orange as indicator."

In the case of sodium salicylate, low results are obtained by this method also, the carbon retaining a small portion of the alkali even after prolonged boiling with excess of standard acid. Warington has also stated that under some circumstances the charcoal retains a little acid, so that low results also would be caused by this effect.

To obviate these errors we have devised the following method, which gives very accurate results: About 1.5 Gm. are heated to dull redness till gases cease to be evolved, taking care not to fuse the carbonized residue. Detach the cooled mass from the crucible as far as possible by means of a glass rod and transfer to a beaker. Boil gently with 50 Cc. distilled water for at least five minutes, and pour the alkaline solution through a filter paper, keeping back as much of the carbon as possible. Boil again with more distilled water, transfer the whole to the filter and wash thoroughly with distilled water. After draining transfer the filter-paper and carbonaceous residue to the crucible, and ignite at a dull red heat until the carbon has been burned completely. Dissolve the residue thus obtained in water and add the solution to the filtrate already prepared. Now add excess of standard acid (say 50 Cc. N/2 H<sub>2</sub>SO<sub>4</sub>), cover with a clock glass, and heat the whole to boiling. In this way any colloidal carbon discoloring the solution is precipitated. Filter again, wash with hot distilled water until the washings cease to

<sup>3</sup> J. C. S., 1875, 925-994.

red den litmus paper. Titrate the unneutralized acid with  $N/2$   $NaHO$ , using methyl orange as indicator. Each Cc.  $N/2$  acid neutralized corresponds to 0.08 Gm. sodium salicylate. The following results show the relative merits of the methods above discussed:

(a) 1.6 Gm. analyzed by the B. P. method required 19.5 Cc.  $N/2$   $H_2SO_4$ , indicating only 97.5 per cent. sodium salicylate. A further 0.4 Cc.  $N/2$   $H_2SO_4$  was used to neutralize the alkali obtained from the carbon residue, making a total of 99.5 per cent. sodium salicylate.

(b) 1.58 Gm. were examined by the U. S. P. method; 19.3 Cc.  $N/2$   $H_2SO_4$ , were neutralized by the alkaline solution, indicating 97.75 per cent. sodium salicylate; a further 0.3 Cc.  $N/2$   $H_2SO_4$  was consumed by the alkali retained by the carbon residue, making a total of 99.25 per cent. sodium salicylate.

(c) 1.5885 Gm. were examined by the new process described; 19.75 Cc.  $N/2$   $H_2SO_4$  were neutralized by the alkaline solution, corresponding to 99.44 per cent. sodium salicylate.

Experiments (b) and (c) were performed on portions of the same sample.

We are indebted to Messrs. Howards and Sons, Ltd., in whose laboratories the experimental work of this note was carried out, for permission to publish these results.

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## PRODUCTION AND EXPORTATION OF MERCURY IN SPAIN.<sup>1</sup>

BY TRADE COMMISSIONER W. M. STRACHAN, MADRID.

Mercury is produced in the Provinces of Ciudad Real, Granada, and Oviedo, but the most important mines are those of Ciudad Real, which are located at Almaden and cover a surface of 485,187 acres. They are owned and operated by the state.

The *Estadística Minera de España* contains some interesting statistics as to the cost of operation of the Almaden mines during the year 1917. In this year excavations were made at 300 sites, at which 2,765 cubic meters were excavated at a total labor cost of \$97,333. The average daily wage paid was \$2.50. The average labor cost per cubic meter was \$35.20. The archwork, solid walls, and masonry

<sup>1</sup> From *Commerce Reports*, August 18, 1919.



erected for the interior support of the mines cost, for materials and labor, including transportation, timbers used for bracing galleries and shafts, etc., a total of \$155,477. Shop expenses for work not let out by contract amounted to \$15,931; the various articles classed as accessories cost \$81,658, and labor not otherwise specified added \$44,498 to the expense.

For labor used in distillation during 1917 the expenditure was \$76,132, and for supplies \$82,148. Ten pairs of Bustamente subliming furnaces, two Cormak-Spirek continuous-movement furnaces for fine materials, and three double-pan furnaces of the same system for coarse ores were employed. In the Bustamente furnaces 7,550 tons of mineral were treated, from which were produced 984,486 pounds of mercury. In the Spirek system 688,795 pounds of mercury were produced from 5,616 tons of ore.

*Output and Quantities Exported.*—The ore on hand at the beginning of 1918 amounted to 60,225 short tons and the production during the year was 11,013, making a total of 71,238 tons. Mineral treated during the year totaled 13,166 tons, yielding 911.7 tons of mercury; thus the metal content was 6.93 per cent.

The exports of mercury from Spain for the years 1908 to 1916, inclusive, were:

Year.	Pounds.	Year.	Pounds.
1908.....	2,353,629	1913	2,746,386
1909.....	3,069,959	1914	2,099,978
1910.....	2,466,935	1915	2,694,394
1911.....	3,293,392	1916	1,752,538
1912.....	2,769,085		

A comparison of the figures of output and export shows that practically the entire production is exported—chiefly to Great Britain.

PHARMACY IN THE RUSSIAN ARMY.<sup>1</sup>

Not the least interesting of many and varied experiences of pharmacy in war on many fronts has been work in Russia, where elements of old Imperial army were operating, side by side, with British units. During the dim days of an Arctic winter one has somewhat exceptional opportunities of studying the details of the pharmaceutical service of another army. The close relations recently existing between the medical service of the British and the Russian (pro-Ally) forces was nothing new, as the British medical profession has always been highly esteemed in Russia.

## HISTORICAL.

So far back as the sixteenth century, and especially during the reign of Ivan the Terrible, English apothecaries were employed at the Imperial Court and held important positions among the Russian noblemen and statesmen. Queen Elizabeth was responsible for sending out the best known of these pioneers—James Roberts, who is still remembered under the name of “Jakobi.” Waliszewski refers to this invasion of Russia by British doctors in his “Life of Ivan the Terrible” (translated by Lady Mary Lloyd). He says that “The whole of these foreign apothecaries could not have induced any native-born Russian to swallow a pill or accept any similar remedy. The moment a Muscovite felt out of sorts he drank a glass of vodka, seasoned with pepper or garlic, ate a slice of lemon, and took a clyster. This was his treatment for every complaint.” Notwithstanding this, British medical men established themselves very successfully in Russia at this period and played an important part in its medical and pharmaceutical history during three centuries. The physicians and apothecaries retained by noble families were held in high honor and richly paid for their services. When they succeeded in effecting cures, estates, serfs, horses, and furs were bestowed on them with truly Oriental munificence. At the beginning of the seventeenth century a state dignitary with the title of *Apothecary boyar* was created, and, with the advent to power of the Romanoffs, the Tsar Michael instituted a pharmaceutical council. This council was an influential body, and appears to have controlled the practice not only of pharmacy but medicine

<sup>1</sup> Reprinted from *The Chemist and Druggist*, September 27, 1919.

as well. The Russian Army of this period was a remarkable body. It consisted chiefly of professional soldiers or musketeers, who lived in a special suburb of Moscow called after them. These musketeers followed various trades in peace time, but received subsidies from the Court and brought up their sons as hereditary soldiers of the Tsar. Like all privileged classes, they became inefficient and mutinous, and were ruthlessly wiped out by Peter the Great, who established an army and an Army Medical Service on the European model. The pharmaceutical council became the medical council, and a State Department under a Scotsman named Erskine, who was the Tsar Peter's personal physician. Owing, no doubt, to the influence of Dr. Erskine, Peter the Great spent large sums in the importation of medical and pharmaceutical educational material and in the equipment of hospitals and schools of medicine and pharmacy. In Peter the Great's army there were two apothecaries on the staff of every general, corresponding to our divisional commanders, and each division had two dispensaries, one for cavalry and one for infantry. Each dispensary had an apothecary-in-charge, with two apothecary's assistants and four pupils to assist him. There were also field hospitals for each division, and each had a field dispensary under the charge of apothecaries. After the death of Peter the Great pharmacy and medicine passed through many phases, and had numerous "ups and downs" until, at the beginning of the nineteenth century, the medical service of the army had been organized into a definite military department, with another Scot, Sir James Wyllie, at its head. Even Wyllie's influence, which was great, was not sufficient, however, to prevent the dual control of hospitals and dispensaries that had crept in during the period between the death of Peter the Great and the accession of the Tsar Paul. In Wyllie's organization was founded the position which still obtains—directors or commissaries of hospitals who are combatant officers, and directors of medical service who are medical men. The former are in charge of all economic and disciplinary matters, whereas the latter are merely responsible for professional and technical duties. On paper the organization of the Russian Medical Service during the Crimean War was excellent, but, like our own, it broke down completely during that campaign. The experience gained, however, led not merely to radical changes in the Russian Army as a whole, but also to a peaceful revolution in the



Russian national life. Serfdom was abolished and national service introduced. In 1869 comprehensive changes were carried out, and the system adopted which was found in Russia at the outbreak of war, and which has continued up to, and since, the revolution. Imperial Russia had the principle of universal service, but certain classes of the community, including doctors and apothecaries, were exempt from service with the Colors in peace-time. Society in Imperial Russia was divided into some fourteen classes. Each class had a definite position in the general community, and all who were government servants were entitled to wear a uniform. Russian officers of combatant services were the dominant class, and the term *ofitser* was actually reserved to them. Officials of the administrative services were not officers, but held in society the position accorded to their relative military rank. The Russian *brach* (surgeon) or *farmatsevt* (pharmacist) held precisely the same position in the Russian army as that occupied by surgeons and apothecaries in our own army prior to 1880. They had medical titles, and relative—but no actual—military rank or powers of command.

#### THE RUSSIAN ARMY MEDICAL SERVICE.

In Russia the Army Medical Service includes the veterinary service, and not only are medical and veterinary stores kept in the same depôts but an actual interchange of duties was permitted, to some extent, between veterinary and medical *personnel*! There is not a special medical corps as in our own and most Continental armies, yet Russian war establishments before the war provided for 3,200 medical officers, 3,800 pharmacists, and over 52,000 medical rank and file. Several writers on the Russo-Japanese War, and on the earlier stages of the Great War, commented on the very generous provision of Red Cross *personnel* with Russian field armies, yet this large body of officers and men had not even a distinctive name and was largely composed of *personnel* temporarily detached from combatant units and other branches of the army. The Russian Medical Service—if we can use the term “Service” for such a heterogeneous staff—was composed of three elements: (1) Military medical *personnel*; (2) military non-medical *personnel*; and (3) civilians.

## MILITARY MEDICAL PERSONNEL.

The medical *personnel* consisted of: (a) Medical officers; (b) pharmacists; and (c) subordinate medical *personnel* (*feldshers* and *nadzirateli*). All surgeons in the Russian army are qualified medical practitioners before entering the army. They are classified in six grades, which correspond with the civil official rank as follows:

Medical Grade.	Corresponding Official Rank.	Corresponding Military Rank.	Civil Title.
1st	Fourth	Major-general	Privy Councillor
2nd	Fifth	Colonel	Actual State Councillor
3rd	Fifth	Colonel	Actual State Councillor
4th	Sixth	Colonel	State Councillor
5th	{ Seventh	Lieut.-Col.	Court Councillor
	{ Eighth	Captain	Collegiate Councillor
6th	Ninth	Lieutenant	Collegiate Assessor

The civil titles conferred certain privileges and were used in official correspondence. All candidates for appointment as *vrach* had to be qualified medical men, but as there were three grades in medical graduates the academic standing of the individual determined the grade to which he was appointed. Persons who had obtained the minor degree of *lekar* were appointed to grade 6, with the rank of lieutenant, whereas those who had obtained the higher degree of M.D. or M.D. and S. (Doctor of Medicine and Surgery) were appointed to the official eighth class, with the rank of captain, and the high-sounding title of collegiate councillor.

## APPOINTMENT OF PHARMACISTS.

Only graduates in pharmacy of the army medical academy or of a Russian university were appointed to commissions in the army. A *farmatsevt* must possess the lower degree of "Provisor" on appointment, but in order to get promotion he must take his degree as Master of Pharmacy. There are four grades of pharmacist, as follows:

Pharmaceutical Grade.	Corresponding Military Rank.	Civil Title.
1st, Glavini farmatsevt	Colonel	State Councillor
2nd, Starshi farmatsevt	Lieut.-Colonel	Collegiate Councillor
3rd, Mladshi farmatsevt	Lieut. or Capt.	Collegiate Assessor
4th, Aptekarshii pomoshniki	Warrant officer	<i>Nil</i>

The Russian military pharmacists are a highly-trained and scientific body of men. In their hands are placed the preparation, supply, care, and dispensing of medical supplies of all kinds, the supervision and charge of military medical store depôts, the charge of analytical and bacteriological laboratories, and of Government factories for the manufacture of surgical instruments and druggists' sundries. The pharmacist official performs only the higher branches of pharmaceutical and administrative duties. The actual dispensing and the bulk of the duties performed by the sergeant and corporal dispensers of our R. A. M. C. are performed by dispensary *feldshers*, a body of subordinates.

#### FELDSHERS.

The *feldsher* is a peculiar feature of the Russian army. The term is applied to the members of a recognized inferior grade of medical, veterinary, and pharmaceutical practitioners. They are found in both civil and military practice, and nothing quite like them exists anywhere except India, where there are two bodies of medical public servants who correspond more or less exactly with the Russian *feldshers*. There are (a) the former apothecaries and (b) the former hospital assistants. The first-named are now called assistant-surgeons and the latter sub-assistant-surgeons. Both are employed in civil as well as in military practice. Both are regarded as qualified to practise outside the army—the apothecaries among all classes and the hospital assistants among the native community. In the Russian army the *feldshers* are the professional assistants of both medical and pharmacist officers, and may take their place just as the assistant-surgeon in India often acts for an R. A. M. C. officer and the sub-assistant-surgeon for an officer of the Indian Medical Service. Medical and pharmaceutical *feldshers* in Russia are trained either before entering or while serving with the army. Only the first class is qualified for civil practice, and this class may be trained in a civil or military medical school. If trained in a military medical school he must serve one and a half years with the active army for each year of instruction received, and the *feldsher* course lasts three years. Appointments are made by district army medical inspectors, and the pharmacist *feldsher* on appointment gets the sonorous title of *mladshi aptechni (feldsher)*. For the second class of *feldsher* soldiers from combatant units are



selected and trained in military medical establishments. *Feldshers* trained in these military hospitals are appointed to companies, squadrons, and batteries, and are junior to the *mladshi aptechni feldshers*, who are employed with higher military formations or in hospitals. *Feldshers* may rise to the rank of "acting officer," a grade somewhat inferior to that of second-lieutenant in our army, but the majority remain non-commissioned officers all their lives. The pharmacist *feldsher* in civil life has limited powers as to the sale of drugs and medicines and is almost exactly comparable with the registered druggist in Ireland.

#### NADZIRATELI OF HOSPITAL SERGEANTS.

The *feldshers* in Russia, like the doctors and pharmacist officers, are only engaged on professional duties. They have no purely military duties to perform. In Russian military hospitals the duties of ward master and hospital sergeant are performed by special *personnel* called *nadzirатели*. Their relationship with medical and pharmacist *feldshers* is peculiar and complicated. They give way to *feldshers* in all professional matters, but are senior to them in all matters of discipline and military precedence. This is typical of Russia, where the representative of executive authority is always superior to the professional or technical official, however highly trained. The result was that a vast host of combatant officers were employed in command of hospitals and military medical formations of all kinds. They had complete control over supply, general management, and interior economy. In peace-time the doctors are barely allowed to treat their patients or the pharmacists to dispense their medicines *secundum artem*, but in war they are given strictly limited powers of command. A *mladshi vrach* when carrying out periodical courses of instruction was not even allowed to command the stretcher-bearers of his unit. A combatant officer was placed in command ostensibly to learn the stretcher drill, but really to prevent a mere *vrach* commanding troops on any form of parade. Under the Republican *régime* this has been entirely altered, and some of the highest military commands are held by doctors.

#### HOSPITAL RANK AND FILE.

Non-commissioned officers for medical formations are drafted from combatant units. As in all other Continental armies a sharp

line is drawn between hospital orderlies and stretcher-bearers. The former are trained in nursing duties, whereas the latter are trained only in first-aid. Subordinate *personnel* for work in pharmacies is specially trained and not employed on other hospital duties. In Russia the regimental system of medical work<sup>2</sup> is developed to the fullest extent, and every effort is made to cure a sick soldier in the regimental *lazaret* or hospital. Each little regimental hospital has a dispensary *feldsher* and usually a well-equipped and well-stocked pharmacy. Pharmacist officers do not serve with regiments in peace or war. They serve on the staff of directors of medical services, have charge of hospital dispensaries, and are employed in depôts of medical stores, laboratories, and factories of medical material. Before the war a certain number of pharmacists were selected for the study of military pharmacy in foreign countries. They were sent abroad at the government's expense, usually for a period of two years.

The Russian Army has three types of field ambulance—regimental, divisional, and brigade. In Continental armies a "regiment" corresponds to our "brigade," and a "brigade" means a group of regiments smaller than a division. The field ambulances are called *lazarets*, and each has one, or more, dispensary *feldshers* who performs all the pharmaceutical duties. Behind the *lazarets* are field-hospitals, which are like our stationary hospitals. Attached to these are field convalescent depôts, which have no counterpart in the British Army. Behind the field hospitals are field clearing commissions corresponding to casualty clearing stations. A pharmacist officer is attached to each field hospital. He has a large subordinate *personnel* of *feldshers* and pharmacy attendants, ranks as a captain, and has the disciplinary powers of a company commander. Sometimes field hospitals are massed together in groups, and the pharmacy is then a very big affair indeed, and the single pharmacist officer has a responsible charge. Pharmacist *feldshers* are employed in bacteriological and disinfection columns, but the pharmacist or his *feldsher* may be found everywhere. One of their most important functions is the care of the

<sup>2</sup> See "Pharmacy in the French and Italian Armies," *C. & D.*, June 7, p. 50, and June 14, p. 64.

## UNITS FOR THE SUPPLY OF MEDICAL EQUIPMENT.

There are two classes of units corresponding to the British advanced depôts of medical stores—field dispensaries and temporary dispensaries. A temporary dispensary has no fixed establishment, whereas a field dispensary is under a *glavni farmatsevt*, ranking as a lieutenant-colonel with a captain as second in command, one to two junior pharmacists, and a large staff of *feldshers* and *attendants*.

A special feature of these field dispensaries is an instrument-repairing shop, with a foreman cutter and trained instrument repairers. Until the revolution the army medical factory at Petrograd was the most important and extensive of its kind in any country.

It consisted of a pharmaceutical laboratory, a surgical dressings mill, and a surgical instrument factory. The latter was in charge of a medical officer of the highest rank, with surgeon-colonels in charge of each section. The medical officers were, however, largely ornamental, and the real work of the factory was carried on by pharmacist officers.

## THE RED CROSS.

Before the war the Russian Red Cross was perhaps the best organized and wealthiest of all the European Red Cross Societies. In addition to the usual private sources of revenue of such bodies it was heavily endowed by the State. The Society had the monopoly of the sale of picture postcards. It received a percentage tax on public and private entertainments, and also the revenue from the sale of stamps on railway tickets and of surcharges on telegrams.

It was very active in peace-time and carried out important relief duties, such as sending detachments to work among the Russian fishermen on the north coast of Norway and among the islands of the Arctic Ocean, but its chief work was the organization and maintenance of lay-communities known as the "Sisters of Mercy of the Red Cross." It employed a large number of pharmacists, as the Red Cross supplied practically every form of medical formation. The Red Cross units worked side by side with those of the regular medical service in the most forward positions. Pharmacists with the Russian Red Cross had all the privileges of their comrades with the regular army. Under the Republican *régime* the pharmacist



was admitted into the class known as the *intelligentsia*, which included all the professional sections of the community and, prior to the Bolshevik upheaval, had the complete control of the executive.

The whole of Russia's political, social, and economic life is now in the melting-pot. British influence was, as has been already shown, the greatest factor in developing the position of medicine and pharmacy in Russia during the past three centuries, and it will be interesting to observe what part will be played in the organization of these twin arts, in the future, by British pharmacy.

M.D., L. P. S. I. (69/91.)

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#### PHILADELPHIA COLLEGE OF PHARMACY, MINUTES OF THE SEMIANNUAL MEETING.

The semiannual meeting of the Philadelphia College of Pharmacy was held September 29, 1919, at 4 P. M. in the Library, the president, Howard B. French, presiding. Twenty-four members were present, with regrets from Joseph L. Lemberger.

The minutes of the quarterly meeting held June 30 were read and approved. An abstract from the minutes of the Board of Trustees for June were read by the Registrar, J. S. Beetem, and approved.

Professor Charles H. LaWall reported verbally for the delegates to the meeting of the American Pharmaceutical Association held at New York City, August, 1919. The College was well represented by its faculty and members. Unquestionably it was a very successful meeting. A number of the members of the College were appointed to various committees, and Professor Lucius E. Sayre, an alumnus and member, was installed as the President.

Professor J. W. Sturmer for the delegates to the Conference of Pharmaceutical Faculties reported verbally that the Conference was somewhat unusual in that there were no "hot fights." One of the most important subjects discussed was that of Four Years High School Requirements for College Entrance—previously agreed upon to become operative September, 1923. A motion to require a four-year course earlier than 1923 was voted down; the other business discussed was mainly along technical lines.

Professor E. Fullerton Cook for the Committee on Nominations

presented the list of nominees for Trustees to be voted for at this meeting. In connection with the report a letter from Edwin M. Boring, one of the nominees, was read, requesting that his name be withdrawn because of physical debility. He had been a member of the Board of Trustees uninterruptedly for forty-one years, and he thought a younger man should be chosen. A number of the members spoke appreciatingly of Mr. Boring's services and hoped he would continue in the services of the College.

Professor Cook requested that the nominations be reopened, and this motion having been adopted another name was placed in nomination. Messrs. Leibert, Thum and Blackwood were appointed tellers. While the votes were being counted, Mr. George M. Beringer reported that the proposed amendments to the charter of the College were now being considered by the state authorities and it was expected that a favorable action would be reported.

Mr. Beringer alluded to the coming Convention to revise the United States Pharmacopœia and thought that we had overlooked the important part the College had always taken in the decennial revisions and suggested that a committee be appointed to present to the Convention in May, 1920, a report embodying the views of the College and recommendations for the revision. It was so ordered, and the president was authorized to appoint the committee.

Dr. A. W. Miller read abstracts from a communication from the University of Bonn, referring to some phases of education resulting from war conditions.

The Committee on Membership reported favorably on six applications for membership in the College. A ballot being taken they were unanimously elected, as follows: Virgil Coblentz, New York City; John G. Eby, Camden, N. J.; J. Howard Houck, Indiana, Pa.; John H. Miller, Lancaster, Pa.; Harold R. Waidelich, Allentown, Pa., as active members, and William G. Schmidt, Philadelphia, as associate member.

Dean Charles H. LaWall reported that up to this date the matriculants in the first-year class in the College numbered 280, the second-year class 160, with increased classes in the postgraduate courses and of special students. There were thirty-five women students enrolled among the number. These figures show a large increase in all the classes.

The tellers reported that Edwin M. Boring, Theodore Campbell

and Aubrey H. Weightman were elected as Trustees for the ensuing three years.

The President reappointed the Committee on Membership, as follows: Freeman P. Stroup, Frank R. Rohrman and O. W. Osterlund, with the Secretary and Treasurer, exofficio.

C. A. WEIDEMANN, M. D.,  
*Recording Secretary.*

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## THE BEECHNUT PACKING COMPANY CASE AND ITS RELATION TO THE "COLGATE PLAN."

By J. E. WALSH,  
NEW YORK, N. Y.

The drug trade is probably very much interested in the general question of price maintenance and price cutting and more particularly in the Beechnut Packing Company case which will come up before the Circuit Court of Appeals probably at its next session.

It was generally supposed that the decision of the United States Supreme Court in the Colgate case determined once and for all the right of any manufacturer to refuse to sell his goods to a price-cutter which has come to be known as the "Colgate Plan" for the protection of resale prices. But this policy is once more the subject of litigation.

The decision of the Supreme Court was that this policy did not violate the Sherman Law. Since it was rendered, the United States Circuit Court of Appeals has decided, in the case of Frey *vs.* Cudahy & Company, that that sales method does not violate the Clayton Act. The Federal Trade Commission, however, claims that it does violate the provision of the Federal Trade Commission Act which prohibits "all unfair methods of competition." They assert that the maintenance of prices by the withholding of supplies from price-cutters is such an unfair method of competition.

The Commission accordingly entered an order against the Beechnut Packing Company, requiring it to desist from this sales policy. From that order the Company has appealed to the United States Circuit Court of Appeals, where the case is now pending. It will be argued on behalf of the Beechnut Packing Company by



Hon. Charles E. Hughes, who argued the Colgate case in the Supreme Court. The Beechnut Packing Company has announced that if the case goes against it, an appeal will be taken to the Supreme Court. Probably the Federal Trade Commission will take such an appeal, if the case goes the other way.

This case raises one entirely new question. The Beechnut Packing Company has extended the "Colgate Plan" and not merely does it refuse to sell to price-cutters, but it refuses to sell to dealers who are supplying price-cutters, even though these dealers may themselves adhere to the suggested price schedule. This additional step in price protection has never come before the courts. So far as this feature of the Beechnut sales policy is concerned, the question at issue is not only whether it violates the Federal Trade Commission Act, but whether it violates the Sherman Law. In so far as the right to refuse to sell to price-cutters is concerned, the only question at issue is whether such a refusal is contrary to the Federal Trade Commission Act. So far as concerns the right to refuse to sell to one who is in turn supplying price-cutters, there are two questions at issue, viz: The first, whether it violates the Sherman Law, and the second, whether it violates the Federal Trade Commission Act.

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## THE SKIN REACTIONS FOR TUBERCULOSIS.<sup>1</sup>

An exhaustive report on the value of the Moro and von Pirquet tests for tuberculosis is given by J. W. Allan (*Glasgow Med. Jour.*, 1918-19, 90-1, 321, 25; Dec.-Jan.). Moro's test consists in rubbing into a limited area of skin an ointment containing Koch's old tuberculin. Von Pirquet's test consists in the inoculation, through an abrasion made in the skin, of a solution containing Koch's old tuberculin. A large number of cases are described, the results presenting considerable variety, and the author concludes that slight or early cases give the best response. Advanced cases with pyrexia fail to give a reaction. Allan concludes in the following words:

"When we get a positive reaction in cases where the bacteriological report is negative, it is to be borne in mind that the failure to detect T. B. is not a conclusive proof that the patient is free from tubercle. The same applies to a negative result from auscultation

<sup>1</sup> Reprinted from *The Prescriber*, September, 1919.

and percussion of the chest. Even a skilled and experienced physician may fail to detect the lesion in a tuberculous lung.

"When we get a positive reaction we may conclude that the patient is affected with tubercle, but it is not necessarily active; it may be latent tubercle.

"The impression left on my mind by the application of these tests is that they are, on the whole, helpful aids to diagnosis. And these cutaneous tests have the advantage that we may use them without fear of doing harm."

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## DISPOSAL OF THE GOVERNMENT STOCK OF PHENOL.

An announcement of importance to the chemical, pharmaceutical and dyestuff industries has been made by the United States government concerning disposition of its large surplus of phenol.

Prior to the signing of the Armistice many millions of pounds of phenol were required by the War Department for the manufacturing of picric acid and other explosives.

As was to be expected the sudden termination of hostilities left an unprecedentedly large amount on hand. It was estimated the quantity was sufficient to cover the peace-time requirements of the United States for four years or more.

The result was a generally depressed market. Phenol being quoted freely much below actual cost without sales. It was a problem for the government to get rid of this great surplus without serious injury to the producers and with the greatest possible profit to the government.

To formulate plans and with the view of coöperating with the industries concerned, a meeting was called during the early part of April at the Chemists Club, New York City, which was attended by representatives of the various interested houses. Pessimism ruled. Many suggestions were made, among others that this vast stock be destroyed with the view of protecting the industry. Finally a representative of the Monsanto Chemical Works expressed faith in Phenol and its future, and gave the opinion that with the proper tariff protection of dyestuffs increased production would result, with a corresponding increased use of phenol.

While nothing definite resulted at the time of the meeting re-

ferred to, it was shortly followed by offers from the Monsanto Chemical Works to buy the entire amount at a price of several cents above the then prevailing market, or to act as the government's agent, thereby permitting the government to receive the benefit of any advance in price.

The War Department officials favored the latter plan, with the result that the Monsanto Chemical Works have received a contract making them sole selling agents for approximately 30,000,000 pounds of phenol.

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### BOOK REVIEWS.

**THE CONDENSED CHEMICAL DICTIONARY:** A reference volume for all requiring quick access to a large amount of essential data regarding chemicals and other substances used in manufacturing and laboratory work. Compiled and edited by the Editorial Staff of the Chemical Engineering catalog. Published by the Chemical Catalog Company, 1 Madison Avenue, New York. Price, cloth \$5.00; leather-bound and thumb-indexed, \$6.00.

The review of a reference book is a difficult undertaking. For proper appraisal of the value of a book of this class it must be used in actual practice over a long period of time.

The book, which was recently issued under the title given above, essays to be more than its name indicates, for it contains so many drug titles as well, that it might easily be termed "A Dictionary of Substances used in Medicine, Pharmacy and in the Sciences and Arts."

To give one who has not seen this book an idea of its comprehensiveness and accuracy can be done only by selecting some one subdivision or group of substances and comparing them with a corresponding list in some other authoritative work. In this case the acids were chosen as the group and the U. S. P. as the authority. On page 504 of the U. S. P. in the table of molecular weights there begins a list of about fifty titles of acids, not all of which, however, are official, either in the text or as reagents. The Condensed Chemical Dictionary lists the titles and descriptions of nearly 200 different acids of greater or less commercial importance and in addition contains more than 200 cross references.



The data given under each heading are of both scientific value and practical importance and are as follows: Physical properties, constants, solubilities, derivation, method of purification, grades, containers, uses, fire hazard and railroad shipping regulations. The information is given concisely yet intelligibly. So far as accuracy is concerned it is probably above the average book of its kind, no book ever published being perfect in this respect. For instance, the following errors were noted in this same group of acids that were selected for critical study and it may be assumed that the remainder of the book will show about the same degree of accuracy.

Under acetic acid, no mention is made of its use in pharmacy or medicine. Under some of the acids, "U. S. P. grade" is mentioned, although the U. S. P. makes no mention of this acid at all except perhaps in the table of molecular weights or under the reagents. Among these are bromic, aminoacetic, anthranilic, butyric, formic (official in N. F.), iodic, molybdic, monochloracetic, ortho-arsenic, oxalic, perchloric, phosphoric (anhydrous), phosphoric (glacial), phthalic, silicotungstic, succinic, sulphurous and valeric.

Under hydrocyanic acid the strength is mentioned as 10 per cent., a dangerous bit of misinformation.

Incorrect strengths are given for hydriodic acid and hydrobromic acid.

Under hypophosphorous acid the formula is incorrectly given as  $H_3P_7O_2$ .

If errors in the other parts of the book are in the same proportion, and quite a number were noticed which it is not necessary to mention, there would be upward of 200 errors in the whole work. This would not be a great number considering the number of titles involved. The errors noted were of minor importance in the majority of cases.

The work is well cross-indexed as regards the names and synonyms of crude drugs and fixed and volatile oils as well as chemicals.

The latter portion of the book is devoted to tables of atomic weights, weights and measures, equivalents temperature conversion tables, specific gravity tables and a list of definitions of units of measurements, many of which would be difficult to find except in highly specialized literature.

The transportation regulations are also fully outlined, both as regards freight and express matter.

The book will undoubtedly find a ready field and the future editions, which will doubtless be found necessary, will probably be free from the defects which usually attend the production of the first edition of such a work.

C. H. LAW.

REVISION OF THE NORTH AMERICAN SPECIES OF XANTHIUM. By Charles F. Millspaugh and Earl E. Sherff, Field Museum of Natural History, Chicago. Publication 204, Botanical Series, Vol. IV, No. 2.

In this splendid monograph the authors have apparently settled numerous matters of bibliography attendant upon North American species of *Xanthium*. A brief history of the work done on these plants by several investigators is first given. This is followed by the characteristics of the genus *Xanthium*, a key to the identification of the species considered, and the characteristics and distribution of twenty-one species. Accompanying the article are seven clear plates, four of which depict the fruit characters of numerous species, the remaining three, the characteristics of the fruiting plants of *Xanthium curvescens*, *X. calvum* and *X. australe*, respectively.

HEBER W. YOUNGKEN.





# THE AMERICAN JOURNAL OF PHARMACY

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DECEMBER, 1919

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## EDITORIAL.

### THE OBLIGATION OF PHARMACISTS TO SUPPORT THE PROHIBITION ENACTMENTS.

The Eighteenth Amendment to the United States Constitution and the legal enactments for the enforcement of prohibition are placing great responsibilities upon the profession of medicine and pharmacy. Upon the former devolves the duty and responsibility of determining when and where and to what extent distilled spirits and wines are to be prescribed as necessary remedial agents. We have faith that the professional spirit, actuating a very large percentage of the medical practitioners, will guide them in the proper discharge of their share of the responsibility. Experience, however, has taught us that there is grave danger that a small minority of the doctors of the country will lend themselves to prescribing alcoholic beverages under the guise of medicines and thus sell their professional inheritance for a mess of potage.

Upon the pharmacists will devolve the double duty, as the sole purveyors of non-beverage distilled spirits and wines at retail, to guard against infractions of the laws by either prescribers or users. It is difficult to see how they are going to escape the additional responsibility thus placed upon them. It becomes the duty of each to fully maintain the honor of his calling and to sustain not only the letter but in his acts likewise the spirit of the law.

Doubtless there will be many temptations offered and the devious ways suggested to those whose moral courage is not strong enough to withstand the tests may lead some into the way of the transgressor. The penalties provided for infractions of the Volstead Act are surely heavy enough to deter any but the most careless or hardened and indifferent from intentional violations.

An insidious form of temptation is now being exploited in the numerous recipes and products that are flooding the market for the production of home made liquors. Special efforts are being made to induce the drug trade to become the medium of distribution for such and the main argument is the prospect of extraordinary profits—as one circular puts it, “a profit that is more than satisfactory.” While some of these may not violate the letter of the law, the evident purpose is to nullify its value in many ways. It is inconceivable that any jobbing druggist who is in harmony with the principles announced by the National Wholesale Druggists Association or who is on the ethical plane of membership in that organization should engage in the distribution of such wares. Still more incomprehensible and even reprehensible would be the selling of these by pharmacists. We can only urge that in deference to the honor and responsibility of their profession that not one should belittle alike his calling and himself by lending his efforts to such nefarious traffic.

The situation that is developing in this country may have a very important bearing upon the professional status of pharmacy. Of one thing we can rest assured, namely, the extent to which the pharmacists under this added responsibility discharge faithfully their duties, will determine their future right to the respect and confidence of the law making bodies and also the recognition accorded by other professions.

G. M. B.

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#### THE WASHINGTON HEARINGS ON PROPOSED REGULATIONS FOR PROHIBITION ENFORCEMENT.

During the first week in December a series of hearings or conferences were held in Washington between the officials of the new Division of the Bureau of Internal Revenue charged with the enforcement of the Eighteenth Amendment to the Constitution and the Volstead Prohibition Enforcement Act and the representatives of the several professions and the various industries that are compelled to use and participate in the distribution of non-beverage distilled spirits and wines. These were presided over by the recently appointed Prohibition Commissioner John F. Kramer.

The hearing on Monday, December 1, was devoted to the sub-

jects of barbers' supplies, perfumes and toilet articles and was well attended by representatives of these industries, their attorneys and a number of chemists employed therein.

The Commissioner in his opening address gave the assurance that it was not the intent of the bureau to interfere with legitimate enterprises nor in any way to cripple or destroy such, but wherever possible to render assistance to all manufacturers who had occasion to use alcohol and whose intent was to obey the law. He read the resolutions adopted by the National Wholesale Druggists' Association and commented favorably upon the attitude of helpfulness to the officials shown thereby and advocated that upon each member of the various trade organizations there be impressed his duty in this respect.

Dr. A. B. Adams, chemist of the Internal Revenue Bureau, spoke of the necessity for eliminating from the barbers' supply trade and manufacture of perfumes and toilet articles certain products that could be and some of which had been already used for beverage purposes. He cited as examples certain hair tonics consisting mainly of alcohol with a trace of quinine or cantharides. He stated that the Department had under consideration a requirement that bay rum and toilet waters would have to be denatured by the addition of some modifying substance. It was explained that tartar emetic to the extent of one fourth grain to the fluid ounce was a suggestion that was being favorably considered by the department and that while at the present they were not prepared to make such statement as a conclusion, it was decided that some modifying substance that would render such products unfit for use as beverages would have to be added before sale to consumer.

Mr. W. L. Crounse, attorney for the National Wholesale Druggists' Association, in addition to the resolutions adopted at the two last conventions of that organization, which had been referred to in the remarks of Commissioner Kramer, gave further assurance of the support of the laws by the members of that body and their purpose to coöperate with the bureau in the enforcement of the law. He also presented the resolutions recently adopted by the Manufacturing Perfumers' Association. He further urged that in the framing of regulations, reasonable provision be made for the disposal of the stocks on hand which represented a very large investment, the loss of which would be serious to the holders of such merchandise.



Mr. H. B. Thompson, attorney for the Proprietary Association, asked that whatever modifying substances may be decided upon that these be such as will not interfere with the nature of any preparation and its intended use and not incompatible with the formula.

Mr. E. C. Brockmeyer, attorney for the National Association of Retail Druggists, stated that the retailers were those upon whom the great responsibility had been placed by these laws and that they must very largely determine the intent of the purchasers. The assurance of this active association in coöperating with the Government in these matters was guaranteed.

The Barbers Supply Dealers' Association was represented by Mr. A. Edlis of Pittsburgh, who read a statement prepared by the Legislative Committee of that organization. It was suggested that the Department "should carefully investigate all applicants for permits to purchase non-beverage alcohol, and that some method be established whereby an applicant must thoroughly establish that his objects are legitimate, other than by the bond that is required by law."

Mr. Wayne B. Wheeler, attorney for the Anti-Saloon League, stated that it was not the intent of that organization to interfere with the proper use of non-beverage alcohol by any industry.

In the general discussion that followed, it developed that the Department's experiments were limited to but a few days' trial of tartar emetic as a modifying agent for bay rum, that no determination had been made as to the toxic action or of its possible systemic effect as a cumulative poison and that no announcement of its use as an approved denaturing agent had yet been promulgated. The consensus of opinion of the expert chemists and technical workers present was that tartar emetic was too violent a poison to be recommended for such purposes and untoward results would likely follow its application in this way.

Dr. Ettner, as chairman of the committee of the Perfumers' Association that had been appointed to make a special study of this subject advised against the use of tartar emetic as entirely too toxic and the use of which might prove a continual source of danger alike to the manufacturers and the unsuspecting user. His committee had under consideration a number of possible modifying substances and experiments not yet completed suggested that several were promising, but until these experiments permitted of a definite decision it was unwise to express a conclusion.

At a conference of the scientific and technical experts present held later in the day, it was decided to request that unless the knowledge justified the crystallizing of opinion in favor of any one agent that the manufacturers and dealers in bay rum and toilet waters requiring such denaturing addition, be permitted to select an alternative substance meeting with the approval of the Division.

The hearing of Wednesday, December 3, was given to the consideration of liquid medicinal compounds and was the most largely attended of these conferences. Commissioner Kramer in opening the meeting stated that the question under consideration was not prohibition as we must look upon that issue as determined but that the question confronting us was that of obedience to the law. He reiterated that it was not the purpose of the Department to interfere, much less to destroy, any legitimate business.

Dr. A. B. Adams, chemist of the Bureau, took the position that there "was no sanctity guaranteed by the fact that a preparation was included in the Pharmacopœia or the National Formulary." He presented the following list of U. S. P. and N. F. preparations fit for use as beverages:

Elixir Aromaticum (Elixir Aromatic).

Elixir Glycyrrhizæ (Elixir of Licorice).

\*Spiritus Juniperi Compositus (Compound Spirit of Juniper).

Tincture Cardamomi Composita (Tincture Cardamom Compound).

Tinctura Lavendulæ Composita (Compound Tincture of Lavender).

\*Tinctura Zingiberis (Tincture of Ginger).

\*Cordiale Rubi Fructus (Blackberry Cordial).

Elixir Anisi (Elixir of Anise).

Elixir Aromaticum Rubrum (Red, Aromatic Elixir).

Elixir Aurantii Amari (Elixir of Bitter Orange).

Elixir Cardamomi Compositum (Compound Elixir of Cardamom).

Elixir Taraxaci Compositum (Compound Elixir Taraxacum).

\*Spiritus Myrciæ Compositus (Compound Spirit of Myrcia).

Tinctura Aromatica (Aromatic Tincture).

Tincture Caramellis (Tinctura Caramel).

Vinum Aurantii Compositum (Compound Wine of Orange).

\*Vinum Carnis (Wine of Beef).

\*Vinum Pepsini (Wine of Pepsin).

Vinum Pruni Virginianæ (Wine of Wild Cherry).

Elixir Glycyrrhizæ Aromaticum (Elixir of Glycyrrhiza, Aromatic).

Elixir Gentianæ Glycerinatum (Glycerinated Elixir of Gentian).

\**Vinum Carnis et Ferri* (Beef, Iron and Wine).

*Tinctura Amara* (Bitter Tinctura).

Those marked with an asterisk he considered as especially prone to misuse and cited the extensive misuse of "Essence of Jamaica Ginger" and an instance where Compound Spirit of Juniper was manufactured and advertised as a substitute for gin.

Mr. W. L. Crounse reiterated the assurance of support from the Wholesale Druggists' Association. Mr. H. B. Thompson called attention to the position assumed by the Proprietary Association some years ago in resolutions adopted declaring that no preparations would be manufactured except for legitimate medicinal use and that the attitude of this association was to be right and also to compel the other fellow to get right and that it stood ready to aid the Government officials by every means possible.

Dr. J. M. Francis, of Detroit, speaking for the Manufacturers of Pharmaceuticals, said that the proper amount of alcohol that was necessary for extraction, solution and preservation of medicinal preparations was the result of generations of experiments and that these had been the factors in determining the percentages of alcohol recommended in the formulas of the Pharmacopœia and National Formulary. He cited essence of pepsin as an example where the amount of alcohol necessary to prevent precipitation of its active constituents and at the same time to maintain a permanent preparation that will not ferment was determined by many experiments. Unfortunately some of these medicinal preparations were of a character to lend themselves to misuse by those who had the drink habit. Certain of these in his opinion did not possess a great importance to the physician yet he conceded that in domestic practice they may be important as household remedies.

Dr. Thomas H. Carmichael, of Philadelphia, speaking as chairman of the committee on Pharmacopœia of the American Institute of Homeopathy, voiced the objection of these physicians to a limitation being placed upon the amount of alcoholic preparations that a dispensing physician could purchase, this limit being placed by T. D. 2940 at two quarts within one year, unless the physician was bonded the same as any other dealer or user of non-beverage spirits. In his opinion at least five gallons should be allowed to each physician, and without a bond being required.

Mr. Samuel C. Henry, President of the National Drug Trade Conference, asked the Bureau to compare the small percentage of



medicinal alcoholic preparations that might possibly be misused for beverage purposes against the quantity used for strictly medicinal purposes. The druggists are bonded and their permits for the manufacture and sale of non-beverage medicinal preparations could be revoked by the Bureau in the event of failure to comply with the requirements of the law.

Mr. E. C. Brockmeyer, counsel of the National Association of Retail Druggists, stated that the brunt of the responsibility would rest upon the retail druggists, and that while many of them were not equipped with laboratory facilities for testing the numerous commodities that enter into their commercial operations, he assured the Commissioner that the Association as a body was ready to co-operate to the fullest extent possible in support of the law and the regulations.

Mr. Wayne B. Wheeler reiterated his statement of Monday that it was not the purpose of the Anti-Saloon League, which he represented, to interfere with any legitimate trade or profession. He pointed out the penalties to which violators of the prohibition laws would be subjected.

Prof. Charles H. LaWall, representing the U. S. P. Committee, stated that the Pharmacopœia had endeavored in every instance to limit the use of alcohol to the amount required for the purpose of extraction, solution and preservation of the preparation. In doing so, two objects were in view—the excessive cost of alcohol and the desire to reduce to a minimum its unnecessary application in medicines.

Mr. G. M. Beringer, as a member of the Committee on Revision of the U. S. P. and the N. F., stated that he was pleased to note that the Commissioner recognized that there was a dual purpose in the Volstead Act, as indicated by its title: namely, not only to prohibit intoxicating beverages but likewise to secure an ample supply of alcohol and promote its use in scientific research and in lawful industries and surely no industry is more essential than that of the manufacture of medicinal supplies, in which alcohol serves as a necessary material. He was grieved to note from the remarks of Dr. Adams, that official preparations of the U. S. P. and N. F. had been linked with proprietary and other substitutes really intended for beverage purposes. The fact that a preparation was included in either the U. S. P. or N. F. indicated that there was sufficient general use for it as a medicinal substance to justify its inclusion as

a standard formula in either of these two legal authorities. From the "Special Notice" in the N. F. he read the following paragraph:

"In accordance with this definition, the standards described in this National Formulary are intended to apply only to such substances as are used solely for medicinal purposes, or when professedly sold or dispensed for medicinal use. They are not intended to apply to substances sold professedly for technical and non-medicinal uses."

A similar statement likewise appears in the U. S. P., and the inclusion of any formula in either of these two standard works indicates its need and use as a medicinal substance. Compound spirit of juniper, which Dr. Adams characterized as an "imitation gin," was placed in the U. S. P. simply as a proper form for the exhibition of oil of juniper, where the physician desired to prescribe same for its diuretic effect.

In more than forty years' experience in pharmacy, in daily contact with physicians and their practice, he had never known of the misuse of this preparation, but had frequently known it to be prescribed in relatively small quantities for its recognized therapeutic activity. Compound tincture of lavender is an ingredient in several other formulas, notably solution of potassium arsenite, where it serves the purpose of distinguishing an otherwise colorless and odorless solution by giving it a distinct color, odor and taste, by which it can be readily recognized and mistakes in its use prevented.

All of the preparations named are more or less commonly prescribed; some throughout the entire country and others only locally, and to forbid their manufacture and to eliminate them from the practice of medicine would cause endless trouble in the adjustment of thousands of prescriptions on file, the renewal of which is necessary. Further such a course would be destructive of the scientific development of pharmacy, which has been along the lines of making medicinal preparations more palatable and efficient.

After this hearing an informal meeting of the representatives of the various associations and firms present was held, with the purpose of endeavoring to frame some constructive suggestions that would aid the Commissioner in framing regulations covering medicinal preparations. Thirteen pharmaceutical and drug trade associations and sixteen pharmaceutical manufacturers were represented in this gathering. As the result of their deliberations, the following recommendations relating to the tentative list of U. S. P. and N. F. preparations submitted at the conference were adopted by resolu-

tion and later submitted to the Prohibition Commissioner as representing the views of pharmacy and the drug trade thereon.

1. That it is the sense of this meeting that none of the U. S. P. or N. F. preparations appearing in the list submitted by the Commissioner of Internal Revenue be eliminated until such time as it is proven that they are being generally used for beverage purposes, especially in view of the fact that the decennial revision of the U. S. P. and N. F. will shortly be made.

2. That we endorse the practice of the Bureau of Internal Revenue requiring a label to be affixed to all medicinal preparations which might be used for beverage purposes, stating clearly that non-beverage alcohol is used in the preparation and that it is a violation of the law to sell or use the same for beverage purposes.

3. That sales by wholesalers and manufacturers of elixirs on this list be made only to those holding permits for the use and sale of non-beverage spirits and duly licensed physicians.

4. That sales of elixirs on this list be made to the consumer only when properly medicated so as to make them unfit for beverage purposes or upon a physician's prescription.

5. That spiritus juniperi compositus (compound spirit of juniper) and spiritus myrciæ compositus (compound spirit of myrcia) be sold to the consumer in the unmodified form only on a physician's prescription.

6. That tinctura cardamoni composita (tincture of cardamom compound), tinctura caramellis (tincture caramel), tinctura aromatica (aromatic tincture), and tinctura amara (bitter tincture) be sold to the consumer in the unmodified form only on a physician's prescription.

7. That tinctura lavendulæ composita (compound tincture of lavender) and tinctura zingiberis (tincture of ginger) be sold in the unmodified form to the consumer in quantities not greater than two fluid ounces at one time and not more frequently than once in ten days to the same purchaser excepting upon a prescription of a physician.

8. That cordiale rubi fructus (blackberry cordial) be sold in the unmodified form to the consumer in quantities not greater than four fluid ounces at one time and not more frequently than once in ten days to the same purchaser, excepting upon a physician's prescription.

9. That the sale of vinum aurantii compositum (compound wine



of orange), vinum carnis (wine of beef), vinum pepsini (wine of pepsin) and vinum pruni virginianæ (wine of wild cherry) be made to the consumer only when properly medicated so as to make them unfit for beverage purposes or upon a physician's prescription.

10. That vinum carnis et ferri (beef, iron and wine) be sold in quantities not greater than one pint to the consumer and only upon the prescription of a physician.

The hearing on Friday, December 5, was devoted to the subject of flavoring extracts. Commissioner Kramer explained that the conference had been called to consider Paragraph (e), Section 4 of the Prohibition Enforcement Act, permitting the manufacture and sale of "flavoring extracts and syrups that are unfit for use as a beverage or for intoxicating beverage purposes."

Mr. R. H. Bond, of Baltimore, speaking in behalf of the Flavoring Extract Manufacturers' Association, claimed that the intent of Congress was that such products should be unfit for use by the normal individual. Doubtless persons of morbid tastes and with intemperate habits might endeavor to use flavoring extracts and many other substances containing non-beverage alcohol to satisfy their abnormal appetites. He urged that consideration be given to the needs of the public, which has been accustomed to the use of flavoring extracts as now manufactured and demands the continuation of such for legitimate purposes.

Mr. Thomas E. Lennen, counsel for the National Manufacturers of Fruit and Flavoring Extracts, said that the manufacturer could not follow his products from the manufacturing laboratory to the ultimate consumer, and if such products were sold without their knowledge by the retailer for beverage purposes, the responsibility for such sale should rest upon the dealer who thus violated the provisions of the law.

Mr. J. G. Caffrey, assistant to the Prohibition Commissioner, advised that such has been and will be the attitude of the Department. Commissioner Kramer, however, stated that the manufacturers should not lose sight of their share of the responsibilities under the law, and that if their sales were made under circumstances from which the seller might reasonably deduce that these were to be used as beverages, the Department would assume that the responsibility rested upon such manufacturer.

Mr. J. L. Clawson, of Philadelphia, claimed that the attention of the Department should also be directed to the consumer who

obtained such preparations and used them improperly as beverages.

Various suggestions as to the size of containers to be used in the sale of flavoring extracts were considered, but no agreement was arrived at by the representatives of this industry that a limit should be placed upon the size of the container by the regulations.

It was apparent to those attending these conferences that the officials realize the enormity of the task imposed upon them to frame satisfactory regulations under the existing laws. It was equally apparent that the trade interests represented are uniformly in sympathy with the Department and desirous of rendering constructive aid in solving the numerous problems involved.

The unusual authority and power granted to the Commissioner, if arbitrarily assumed, would enable him not only to interfere with legitimate industries, but to seriously cripple them and prevent their development or even destroy them.

Take the perfume industry as an example: the American manufacturers have shown a remarkable development in this art, not only in quality but likewise in the growth of the industry and the amount of products exported. By discrimination or unwise regulations, this branch of American manufacture may be seriously handicapped. The Department should be exceedingly slow in framing regulations that are not absolutely called for that would interfere with this industry. This applies with even greater force to the manufacture of pharmaceutical and medicinal preparations.

It is sincerely hoped that in questions of vital importance to the public at large and to the industries concerned, the officials will accept the advice of representative men whose many years of acquaintance with trade and professional practices should be a guide to the Department in this work. To unnecessarily interfere with the necessary supplies of commonly used medicines would be an unjustifiable exhibition of authority.

G. M. B.

## OPIUM IN CHINA.

BY YING C. WONG.

## INTRODUCTION.

With the introduction of Western ideas, and the pushing eastward of the West with mingled awe and inquisitiveness for its own advantage, China has been, during the last twenty years, facing many reforms, changes and struggles which might be of practical use in saving her from degradation and corruption. One of the many struggles is the suppression of the opium evil, which has cost the nation billions of dollars, and more important than that, has led millions and millions of her strong citizens into wreck and misery. She has fought this gigantic moral conflict which has raged over a territory comparable in size to the United States. Hundreds of thousands of officials, gentry, merchants, students and farmers have been drawn into it. Blood has been shed and property has been destroyed on a large scale. Its victory at the end would undoubtedly be the most wonderful one on a vicious private habit that the world has ever known.

## HISTORY AND CULTIVATION OF THE POPPY.

The poppy does not seem to have been indigenous to China, and has been unknown previous to the Tang dynasty (618-907 A.D.) It was then introduced by Arab traders as a soporific drug, and the plant, either as a handsome garden flower or as a useful medicine, is repeatedly mentioned down to the seventeenth century. In 1621 tobacco-smoking and tobacco cultivation were introduced from the Philippine Islands. In the time of the last Ming Emperor (1627-1644 A.D.), tobacco-smoking was as vigorously denounced and prohibited as opium-smoking was a hundred years later. Opium-smoking was first heard of in the fourteenth century. In 1729 there was an edict issued which prohibited the use of opium and ordered the closing of the smoking dens. The importation of opium was forbidden under very severe penalties. The opium on seizure was to be burned, the vessel carrying it confiscated, and the Chinese salesmen were punished with death. Late in that century, because of the British East India Company's pushing its Bengal opium into the various ports, the habit took root in all parts of the country. The British found that it was a lucrative trade and never gave it



up. The total gain from Indian opium, that is the amount paid by China for that commodity above its cost price between 1773-1906, has been estimated as two billion dollars. In about 1840, the Emperor became so alarmed at the inroads of the poison, that he appointed Lin Imperial commissioner at Canton with orders to put down the trade. His efforts brought him into collision with the British traders and his destruction of ten thousand chests of opium precipitated the first Opium War. It ended in England's forcing on China a humiliating treaty which heavily indemnified the traders for their losses. Besides this, the concession of Hong Kong was given to Great Britain. The grave contention about the opium trade, was, however left untouched, and the Chinese Government, with the great trouble and danger of the Tai-ping rebellion (1850-1864) on their hands, irritated by continuous opium-smuggling, challenged a second Opium War in 1857, resulting in the Treaty of Tientsin which bound the Chinese Government not to interfere with, nor limit the introduction of Indian opium into the Empire.

Until this time the government had not tolerated the cultivation of the poppy plant, but now, rather than see the country drained of silver to buy of India a narcotic that could easily be produced on her own soil, the government removed its restriction, and the poppy spread with great rapidity. In the end, six sevenths of the opium consumed was home-grown.

In most parts of China, the cultivation of the poppy spread at an alarming rate; the interior provinces shut away by mountains from the commercial highways, especially were given over to poppy growing. The reason is that opium is the one crop that can be gotten to market without most of its value being eaten up in the cost of transportation. To the farmers of Yunnan, Kweichow, Szechuan, Shensi, and Kansuh, opium is the only road to the market, just as in Washington's time, whiskey was the only route by which the trans-Allegheny settlers could get their surplus corn to tidewater, and poppy prohibition stung some of them into resistance just as the Federal taxes on spirits led the farmers of Western Pennsylvania into the Whiskey Rebellion of 1798.

#### SOME INTERESTING SYNONYMS AND THEIR APPLICATION TO THE DIFFERENT GRADES OF OPIUM.

With the spreading of the growing of the poppy, the immense importations of foreign opium, and the popular use of the drug by

the people, opium in China was given many very interesting names. The principal ones are "Kung-yen" (public-smoke), "Kung-kao" (public-extract), "Kung-tu" (public-earth), and "Kung-pan-tu," from the Chinese name for the East India Company, Kung-pan-ya. These terms are also used for Patna opium and for the "first-class" quality. Another name for Patna opium is "Ta-tu" (big-earth), while the Malwa is known as "Hsiao-tu" (small-earth). "Yen-tu" (smoke-earth), "Yang-tu" (foreign-earth), and "Kwang-tu" (Canton-earth), are common names for opium, while "Hei-tu" (black-earth) is a slang term for it. The commonest colloquial term, however, is "Yang-yen" (foreign-smoke). The foreign drug is considered the best, and is not noticeably replaced by the native article, although this latter is called "Chuan-tu" (Chuan-earth), and in favorable years can be produced at about half the cost of the Indian drug. It is made to imitate Malwa opium, and has been found to contain 6.94 per cent. of morphine. Yunnan opium, and that from Kwei-chow, are called "Nan-tu" (southern-earth), while that from Kansu, Shensi and Shansi is called "Hsi-tu" (western-earth). These all represent good qualities of the native drug.

#### OPIMUM SMOKING.

During the latter part of the nineteenth century, or since 1860, the luxury use of opium spread with appalling rapidity. Fifteen years ago, seventy times as much opium were used as that used in 1800. Annually twenty-two thousand tons of the drug were absorbed, most of it converted into thick smoke and inhaled by a legion of smokers estimated to number at least twenty-five millions. In Yunnan, the principal inquiry in matrimonial negotiations was, "How many opium pipes in the family?" this being a certain indication of its financial standing. Whole populations, including officials, gentry, students, merchants, and farmers had given themselves up to the seductive pipe and were sinking into a state of indescribable lethargy, misery and degradation. The pipe has a peculiar seduction for these people, because their lives are so bare of interest. The lack of indulgence in the innocent companionship of men and women which contributes such a charm to life is the chief cause which led the Chinese to such vice. They take it as a relief from the dreary flatness that results from sacrificing most of the things that make life interesting in the foolish endeavor to maintain the

largest possible number of human beings. Under their family system that tempts them to multiply without regard to prospects, they have pruned away much which lends value to life. Another cause is poverty. They often have so little food that any drug which removes first the pangs of hunger, and later the healthy cravings of appetite, seems a boon to them. In addition to this there is the feeling of peace and well-being that often accompanies the smoking of opium and it is not difficult to see why the indigent Chinese use it. It is for the same reason that the Western people administer morphine to relieve pain and weariness. The effect desired by the opium smoker is not that of slumber filled with fascinating dreams, but a condition of dreamy wakefulness in which the mind is lifted out of the petty annoyances and cares of life.

The prepared drug is called "Yen-kao" (smoke-extract) or "Shu-yen" (boiled-smoke), and is prepared by mixing the ashes from opium pipes with the raw opium, which facilitates the making of the infusion. This is further filtered and evaporated to the consistence of a thin extract, which is combustible in the opium-pipe when held in the flame of a small oil lamp. The opium is smoked from this special pipe, the stem of which is usually from 20 to 24 inches long, generally made of bamboo, at the lower third of which there is placed a bowl, usually of red clay, through which a minute hole runs down into the stem. The extract is usually made by the keepers of the opium-dens, but rich people usually make their own extract.

The amount smoked varies with various smokers. Kane gives the tabulated statement of the daily dose of 1,000 smokers; 646 varied between 16 and 128 grains; 250 from 160 to 320 grains; 104 from 480 to 1,600 grains. To obtain the desired effect 5 grains seem sufficient for a novice, while old smokers need as high as 290 grains. Among Americans this vice is of relatively recent origin and the average American seems to consume more than the average Chinese to obtain the desired effect.

The addiction to this habit varies somewhat with different individuals, and it seems that it depends a great deal upon the idiosyncrasy of the individual. However, after one has smoked a few times the habit becomes established. As a result of this, there is physical and moral deterioration, insomnia develops, sexual degeneracy supervenes, and there is lack of moral control. Some had smoked to the extent that they had Po-chia-shang-shen ("broken



up the home and destroyed the body"). The confirmed opium smoker is described as black-faced, weak-voiced, watery-eyed, brown-teethed, with prolapse of the bowels, and prospects of an early death.

One would naturally be surprised at the large doses quoted above, and that such did not produce death. As compared with the other forms of opium addiction, smoking takes longer time to form a real habit, works less physical and mental injury when once formed and is easier to cure. In smoking, the morphine is not all consumed and a large amount remains in the ash. Amounts of opium are smoked which, if taken by the mouth would certainly produce death. The burning of this extract in an incomplete manner, as practiced by the Chinese smokers, yields a smoke containing sundry empyreumatic compounds unknown to the chemists, but producing by absorption into the pulmonary vessels a stimulant, or some indescribable effect unknown to all but the actual smoker.

Though opium had been used as an analgesic to a certain extent, its place among the medicines is quite unimportant among the Chinese. Being a poison, it has been employed for suicidal purposes, and this is most common among women. When the crop is in the unhappy women who have been waiting for it (for women abhor a violent death) seize their opportunity. When the drug was at its highest point of abundance, such suicidal cases happened every day and everywhere, for that was the only poison within her reach when some poor woman thought to end her sorrows. However, the continual rise in the price and the restricted sale of opium have manifestly decreased the number of attempts at suicide by the taking of this drug.

On account of the prohibition, and the realization of the deadly effects of the poison, smokers began to seek means for getting rid of the habit. The failures were far more frequent than the cures, from the fact that it requires the exhibition of great will power on the part of those whose will power had already been weakened and partly enslaved. Tonics, stimulants, anti-opium pills, anti-opium tea, etc., have been put up by physicians and others to suit the purpose. Many of these did more harm than good, because they contained morphine which is a more severe narcotic. Thoughtful smokers with strong will power and self-control, have been successful in ridding themselves of the habit just by decreasing the doses day by day until there was a complete extinction of the opium.

However, the use of tonics and stimulants under careful supervision of a competent and conscientious physician, combined with the provision of good food for body and mind, with restraint and disciplinary measures in certain cases would greatly aid in curing the habit.

#### SUPPRESSION OF THE POISON.

The cultivation of the poppy which had been once spreading at an alarming rate, and the vice of opium-smoking which had been degrading the people with great rapidity, have come to the light of hopeful stoppage. The famous Anti-opium Edict issued by the Empress Dowager September 20, 1906, which commanded that the growth, sale, and consumption of opium should cease in the Empire within ten years was the opening gun in the most extensive warfare on this vicious private habit that the world has ever known. Since the Edict radiated from the apex of the governmental hierarchy at Peking, the higher officials were in general more vigorous in enforcing the Edict than the lower. In many cases viceroys and governors have been dismissed for lack of zeal, and new trusty men have been put in their places to put through this governmental policy. Along with these governmental forces, Anti-opium Societies sprang up, standing shoulder to shoulder with the government in the fight.

Because of the prohibition of poppy growing, most of the acreage was turned over to wheat and cotton cultivation, and it was a striking fact that in four of the great poppy growing provinces the prohibition was followed by a season of wonderful harvests. This shows that the sacrifice for the reform was well repaid. The wheat crop ran from 28 to 40 bushels to the acre. This and the restoration of so much land to food-growing have made food more plentiful and cheaper than ever before. New trades have sprung up, with the result that merchants who went out every summer to buy the drug are now trading in goat skins, donkey hides, pig bristles and human hair. In these provinces, Chinese experts in the agricultural schools are by their experiments showing the farmers that they can grow beets, potatoes and cotton instead of opium. In Fokien, cotton seeds were introduced from the United States Department of Agriculture for experimental planting in the fields once given over to poppy growing. Thanks to this, the production of cotton and wheat in China have been recently greatly increased.

As an earnest of its resolve to shake off its lethargy, and to make the Edict efficient, it was found necessary to clear the situation by establishing testing bureaus at Peking and the provincial capitals. The suspect was obliged to submit himself to a rigid test. After being searched for concealed opium, he was locked up for three days in a comfortable apartment and supplied with good food, but no opium. If he held out, he was given a clean bill of health, for no opium smoker can endure three days' separation from his pipe. By this means, certain highnesses were summarily cashiered. In the army both officers and common soldiers have been beheaded for obdurate indulgence.

With such a great and deep-rooted vice, aided by the continued importations from foreign countries, immediate stoppage was found impossible. Opium was allowed to be sold by licensed dealers to persons holding permits for some time. Such permits were issued only to those who proved to have the opium-smoking habit, and had to be posted outside the places where the opium was to be smoked. The smoker had to renew his permit every three months and a less amount was to be supplied each time. After buying the opium, he had to carry it through the street openly.

Under the coöperation of the Anti-opium Societies with the officials, the Edict was enforced with fruitful results. The societies collected and broke up paraphernalia seized in their raids or given up by reformed smokers. The stock on hand was from time to time stacked up in a public place and solemnly burned. In one of the burnings, the pipes, bowls, plates, lamps and opium boxes sacrificed by fire were upward of twenty-five thousand. In one city alone seven thousand dens have been closed. Thanks to these endeavors, the number of opium smokers has been remarkably decreased. Hardly any but low-class people now smoke opium. It has been estimated that between one and two million places for the smoking of opium have been removed. A national conscience has begun to show itself and the slave of the pipe has been put to the blush. The accomplishment during the ten years allowed for the cleansing of the land from the opium habit, as stated in the Edict, has surpassed all anticipations. The production of opium in the country has been cut down about 90 to 95 per cent. or almost entirely.

The finish of the poppy growing is in sight, but the imported Indian opium is the difficulty of the situation. In 1907 when the exports of Indian opium to China aggregated 3,400 tons, the British



Government agreed to reduce this total export at the rate of one tenth, or 340 tons, a year until 1911, with the assurance that the reduction would be continued in the same proportion beyond that period provided the Chinese Government had within the period cut down its home production in like degree.

In 1910, the Chinese Government desired to shorten the period of nearly eight years, during which India was to continue to send opium to China. The Chinese Senate and the Christian people of Great Britain in a series of most earnest resolutions appealed to the British Government to release China from her treaty obligations to receive Indian opium. The smoking people were likewise becoming very restive in seeing their little patches of opium destroyed while tons of the poison were permitted freely to enter Chinese ports.

In 1911, yielding to the accumulating pressure, England entered into an agreement with China whereby she consented to the imposition of a higher duty on opium, agreed not to convey opium to any province of China which had suppressed the cultivation and import of native opium, engaged to cut down exports of opium from India until the complete extinction of the trade in 1918, provided China kept up the suppression of opium growing.

The time for the entire suppression of the poppy growing within the country, and the complete extinction of the trade has expired. But the poison is still found in the hands of foreign dealers. In order to bring it to an immediate close, the government has been undertaking to burn all the opium stock, amounting to about \$25,000,000, recently purchased of the foreign dealers and to issue a mandate for the immediate and complete suppression of the opium traffic throughout the country. The following statement, which is one of the resolutions of the Society for Constructive Endeavor of Shanghai (represented by more than fifty national organizations) on the subject of government destruction and suppression of opium, clearly indicates the public opinion and sentiment of the people:

"The Society has learned with profound satisfaction the decision of the government to burn all the opium stock recently purchased of foreign dealers, and to issue a mandate for the immediate and complete suppression of the opium traffic throughout China, and this decision recognizes and accords with unmistakable public sentiment against the revival of the opium traffic in any shape or form, and therefore merits and receives the full support of the public in-

terest and public conscience not only in China, but approved by enlightened minds the world over."

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### QUERY: THE YEAR BOOK OR AN ABSTRACT JOURNAL, WHICH?<sup>1</sup>

#### ANSWER: BOTH.

BY JOSEPH W. ENGLAND, PH.M.,

PHILADELPHIA, PA.

Your chairman has asked me to discuss the resolutions recently passed by the New York Branch, copy of which has been sent to the Philadelphia Branch, and I hesitate to do so because of my position as secretary of the executive committee of the Council; but since the question at issue is being publicly discussed, the following personal opinion is presented:

The resolutions of the New York Branch are, in brief, as follows:

"That the Executive Committee and Council take speedy action to submit the proposition of issuing either the *Year Book* or a monthly *Abstract Journal* to a vote of the membership of the Association in the form of a special postcard referendum, and that the postcard ballot give to each member the opportunity of voting on one of several options, such as, keeping the annual dues at \$5.00, or raising them to \$6.00, or to \$7.50, each under certain specified conditions regarding the issuance or non-issuance of the publications of the Association."

The proposal of a referendum is not new. It was proposed at the New York meeting, both by the Association and by the Council.

<sup>1</sup> Read before the Philadelphia Branch, *A. Ph. A.*, November 11, 1919.

The Association first favored a referendum on an increase in dues. Later, the Council first decided for a referendum on an increase in dues with reference to the issuance or non-issuance of a monthly *Pharmaceutical Abstract Journal* or the *Year Book*, and the next day it reconsidered its action and referred the question to the Executive Committee for consideration and report to the Council. The minutes of this meeting of the Council were read at the final session of the Association (August 30) and amended by the Association as follows:

"That the Association reconsider its action in the matter of a referendum on an increase in dues, and that the question *in all its bearings* be referred to the newly created Executive Committee of the Council for investigation, and report to the Council for approval, and later, report its findings at the first general session of the Association next year." (*Journ. A. Ph. A.*, Oct., 1919, 848.)

"The minutes of the Council, as amended, were then approved." (*Journ. A. Ph. A.*, Oct., 1919, 848.)

Obviously, the Association having decided against a referendum on an increase in dues "in all its bearings," which includes the issuance of publications, it is hardly in order, now, for the Council or its Executive Committee to take a special postcard referendum on the subject and the question must await decision until the next annual meeting of the Association in 1920. The Council cannot supersede the Association.

Hence, it is not necessary to discuss the question of taking a referendum vote, but it is entirely in order to discuss the future of the *Year Book* and the proposition to replace it with a monthly *Abstract Journal*.

Personally, I believe that Mr. Gathercoal's suggestion of a monthly *Abstract Journal* has much to commend it. The pharmaceutical research workers of the Association are entitled to the promptest possible information of all developments in pharmaceutical research, but is it necessary to abandon the *Year Book* to give this?

R. W. Terry has suggested that the JOURNAL give, each month, a bibliography or list of titles of articles of current pharmaceutical literature, and H. V. Arny has suggested that the JOURNAL give an "Index Pharmaceuticus," or index of articles of current pharmaceutical literature; but why not give in the JOURNAL, monthly, a list of the titles of original articles of pharmaceutical periodicals, for-



eign and domestic, *together with the briefest possible description of their scope* analogous to the *Chemical Abstracts* of the American Chemical Society, but even briefer, and also, continue the publication of the present *Year Book*?

Such a procedure would be entirely practicable. The field of pharmaceutical research is comparatively limited and it would not take many pages of the *JOURNAL*, each month, to cover the field. It would be less expensive, also, to utilize the *JOURNAL* as the medium of expression, than to publish a separate periodical, while to the practical worker the manner of publication would be immaterial so long as he got the gist of the matter and could refer to the original promptly. Such a department of the *JOURNAL* could be called "Pharmaceutical Abstracts" or "Current Pharmaceutical Literature."

The function of a *Year Book* is radically different from that of an *Abstract Journal*. The object of the *Year Book* is to give an annual, systematic review or digest of pharmaceutical progress in orderly, logical sequence, fully and completely.

It is unthinkable that the *Year Book* be abandoned. It fills a niche occupied by no other book in pharmacy as a work of reference. For sixty-seven years, the Association has published its "Report on the Progress of Pharmacy" as contained in its former *Proceedings* and its present *Year Book*, and these volumes constitute the history of the development of American Pharmacy and give to the American Pharmaceutical Association a prestige that is international, as well as national.

The Association cannot afford to discontinue the publication of the *Year Book* which, under the able and brilliant editorship of H. V. Arny, our Reporter on the Progress of Pharmacy, is maintaining the highest traditions of the Association. Its continued publication is essential, not only for the sake of the pharmaceutical research workers of today, but also, as a duty the Association owes to posterity in furnishing a recorded history of the development of American Pharmacy.

The solution of the problem of the *Year Book* vs. an *Abstract Journal* would, therefore, seem to be to publish both—the former, as heretofore, and the latter as a department of the *JOURNAL*.

But the question arises: Can the Association afford the increased expense? And I am frank to say that I do not believe it can without increased revenue, but I do believe that increased rev-

enue can be readily gotten by sufficiently increased membership, provided the present system of annual dues, which is the same today as it was in 1852 when the Association was founded, be properly modified.

As a matter of fact, the question of the finances of the Association is the crux of the whole situation. In the first place, it should be stated that the finances of the Association are in excellent shape—they have never been better, but the expenses of the Association are constantly increasing.

In common with individuals everywhere, the Association has felt the pinch of the high cost of living, and its activities have been restricted, instead of being expanded, as they should be. As President LaWall has said, "There is no question as to the value of our organization to the majority of the members who belong to it. There is no doubt either, as to the great increase in the overhead costs to the Association, and if things continue in the same proportion, we shall soon have a deficit in the treasury."

It may be of interest to state that, during 1918, the receipts of the Association, excluding those belonging to the A. Ph. A. Research Fund (which were covered into the Fund on January 1, 1919) and the interest on investments, were but slightly in excess of the disbursements; there was no deficit.

Of these receipts about 60 per cent. came from the annual dues of members, about 25 per cent. from *Journal* advertisements and about 10 per cent. from the National Formulary, and the balance from other sources.

If the receipts from interest and other sources be taken into consideration, the Association may be said to be in excellent financial condition; but the point is that *there is a positive need for more revenue if the Association is to do the kind and volume of work it must do to progress.*

A largely increased membership is most desirable, not only because it will mean increased revenue and relatively less "overhead expense," but also, because it will make the Association more fully representative of American Pharmacy, give it greater influence and prestige, and enable it to better promote the objects for which it stands. Hence, the necessity for "a nation-wide, intensive drive for increased membership, utilizing every agency at the command of the Association, but all working under one head," as suggested by E. L. Newcomb. Such a drive should be, of course, "modern, strongly

organized, efficiently managed and adequately financed," and also, along broad, comprehensive lines and in close coöperation with the State Associations (on the 51 per cent. basis plan recently adopted) and the War Veteran's Section.

But something more is needed. What the Association needs to-day, most of all, it seems to me, is an entire revision of its system of membership so that *the dues shall be graded by the cost of the service rendered to each member.*

For example, I do not believe that the 3,000 members of the Association want or use the Year Book; hence, every book printed and distributed in excess of those needed is just so much money needlessly wasted. Why print 3,000 books and waste, say 2,000? Why not require the 1,000 who want the book to pay, say \$2.50 each for it? By so doing, the book would cost the Association nothing, and the Association would save several thousands a year.

It may be claimed that the membership can be increased to a point where the present dues of \$5.00 would pay for all that is now given for that amount, because with increased membership the relative overhead expense would be "cut" and more net revenue obtained; but the difficulty is that the present *fixed* cost of each member (and this is constantly rising) is so high, that an exceedingly large number of new members would have to be gotten to yield the revenue desired, and this is improbable. On the other hand, if the annual dues are increased to \$7.50 for *all* members for *all* publications, as proposed, many will resign and fewer new members will be gotten than could be otherwise.

The logic of the situation, therefore, suggests that the Association establish several classes of members, as follows:

1. Members or Active Members who will pay \$5.00 dues and receive the JOURNAL only.

2. Contributing Members who will pay \$7.50 dues and receive both the JOURNAL and the Year Book.

3. Corporation Members who will pay \$25.00 dues and receive special services in the way of information, reprints, etc. (similar to that offered by the American Chemical Society).

4. Associate Members who will pay \$3.00 and receive no publications; this could include drug clerks, soldier and sailor pharmacists, etc., who wish affiliation for prestige only.

Some such plan as this would be modern and businesslike. It would mean a square deal both for the membership and the Associa-



tion. Each member would get only what he wants and is willing to pay for, and the Association would get what it pays for the service it renders to its members; and would have a reasonable sum of money for expense that would permit an expansion of its activities limited only by the size of its membership.

But, as you know, the whole question of annual dues, finances, membership, etc., is now in the hands of the Executive Committee for consideration and report to the Council (and later to the Association) and I feel that I am but expressing the wishes of the Committee when I say that the latter will gladly welcome any and all suggestions reflecting the wishes of the membership to the end that the fullest light may be had on the subject, and a satisfactory decision reached.

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## THE STATUS OF LEGISLATION BEARING UPON MILITARY PHARMACISTS.

BY E. FULLERTON COOK, PH.M.,

PHILADELPHIA, PA., SECRETARY N. P. S. A.

### THE SURGEON-GENERALS ASK FOR COMMISSIONS FOR PHARMACISTS.

During the meeting of the American Pharmaceutical Association in New York, a letter from the Surgeon-General of the United States Army, Dr. Ireland, was read, in which he announced his intention of asking for the organization of a Medical Service Corps for the United States Army and agreed to provide a limited number of commissions for pharmacists in this corps. Carrying out this promise, Dr. Ireland appeared before the Committee on Military Affairs of the House of Representatives on October 3, and after presenting the need of a service corps, was asked to draft a bill which would supply this need. In speaking before the Committee, Dr. Ireland said:

"I would like to have a few minutes to put up a proposition which I believe is greatly in the interest of the efficiency of the Medical Department. This could be accomplished without expense. For some time we have needed a service corps. During the Civil War field hospitals and ambulances were authorized along about 1862, and at that time by act of Congress and by order of the War Department line officers could be detailed to act as our quarter-

masters at our general hospital and as commanders of ambulance companies. They did work of a nonprofessional character. It is needless for me to tell the committee that the quality of officers we want to do that work will not come to the Medical Department in time of active operation. They, of course, want to remain with their command. That has resulted in the medical officers commanding the ambulance companies, having charge of our transportation, acting as adjutants of our hospitals, being the quartermasters or property officers or mess officers in our large institutions.

"It has taken an enormous number of these highly trained medical officers for nonprofessional work, which is a great wastage of material, as they ought to be taking care of the sick and doing professional work. We would like to make enlistment in the Medical Corps popular by offering men a commission, after five years' service, in a service corps. They must come in the Medical Department and serve as enlisted men for five years, and at least three years of that time should be in the grade of noncommissioned officer, indicative that they have made good as enlisted men. After a certain length of time they could be examined under regulations prescribed by the Secretary of War, and commissioned in the service corps. They would be our adjutants, property officers, mess officers, pharmacists, and perform all such nonprofessional work. The Medical Corps is willing to give up officers in the grade of major, captain, and first lieutenant sufficient to organize that corps. We ask for one service corps man for every two thousand enlisted men, and we will give up enough of our seven-tenths of 1 per cent. of medical officers in the Medical Corps to organize that service corps. That would make enlistment in the Medical Corps very attractive. It provides a future for the enlisted man.

It would solve another problem which has bothered the department for a long time. There is some need for pharmacists in the United States Army. They have them in the Navy. They have a pharmaceutical corps. There is not a sufficient need to organize a pharmaceutical corps in the Army, but if we have a service corps we would take care of a certain number of pharmacists in that service corps."

The chairman of the Committee then asked: "That statement that there is no need for a pharmaceutical corps in the Army is not admitted by the pharmacists, is it, General?"

General Ireland replied: "I think they believe, and have believed

for many years, and have insisted for many years, that we should have pharmacists in the Medical Department; but I have had a talk with the pharmacists, and they have agreed that if we can secure a service corps and will give them a limited number of pharmacists, they will accept that and be satisfied. I believe the pharmacists of the country will accede to what I have said."

Dr. Ireland subsequently presented the following plan:

"ARMY REORGANIZATION—PROPOSED SECTION RELATING TO MEDICAL SERVICE CORPS.

"A Medical Service Corps is hereby established, which shall be a part of the Medical Department, and shall consist of a commissioned force and an enlisted force.

"The commissioned force of the Medical Service Corps shall consist of officers, the total number of whom shall approximately be equal to one for every 2,000 of the total enlisted strength of the Regular Army authorized from time to time by law, and shall be distributed by grades as follows: Majors, 25 per cent.; captains, and first lieutenants, 75 per cent.: Provided, That if by reason of a reduction by law of the authorized enlisted strength of the Regular Army the total number of officers in the Medical Service Corps commissioned previously to such reduction shall for the time being exceed the equivalent of one for 2,000 of such reduced enlisted strength, the total number of said officers shall be reduced to said equivalent in the manner prescribed by the first proviso of section 10 of the National Defense Act approved June 3, 1916 (39 Statutes at Large 166), respecting the Medical Corps: Provided further, That the number of majors in the Medical Corps authorized by section 10, of the National Defense Act, approved June 3, 1916 (39 Statutes at Large 166), shall be diminished by the number of majors in the Medical Service Corps, and the number of captains and first lieutenants in the Medical Corps shall be diminished by the number of captains and first lieutenants in the Medical Service Corps: Provided, however, That nothing in the last preceding proviso shall be held or construed so as to discharge any officer from the Medical Corps of the Regular Army or to deprive him of the commission which he now holds therein.

"The officers of the Medical Service Corps shall be utilized so far as practicable in the performance of the business and adminis-



trative functions of the Medical Department, to wit, as adjutants of Medical Department units, registrars of hospitals, pharmacists, medical property and supply officers, medical finance officers, hospital mess officers and in other positions where the special professional training of medical officers is not required.

"The officers of the Medical Service Corps shall be appointed by the President, by and with the advice and consent of the Senate, from among the noncommissioned officers of the Medical Service Corps and of the Veterinary Corps who shall have served not less than five years in one or both of said corps, including service in the Hospital Corps and in the enlisted force of the Medical Department, and not less than three years in noncommissioned grades, who shall at the date of appointment be citizens of the United States and not more than thirty-two years old, and who shall have been found qualified by a board of not less than three officers of the Medical Department for the duties of commissioned officers of the Medical Service Corps upon such examination as shall be prescribed by the Secretary of War: Provided, That persons who, having previously been enlisted men in the Medical Department of the Army for not less than five years, shall have served honorably as commissioned officers in the Army of the United States during the war with Germany, shall until July 1, 1920, be eligible regardless of age for appointment to original vacancies in any grade in the Medical Service Corps created by this section.

"The enlisted force of the Medical Department is hereby merged into the Medical Service Corps, and from and after the passage of this act shall constitute and be known as the enlisted force thereof. The total strength of the enlisted force of the Medical Service Corps shall be approximately equal to, but not exceed, except as provided in section 10 of the national defense act approved June 3, 1916 (39 Stat. L., 166), the equivalent of  $5\frac{1}{4}$  per cent. of the total enlisted strength of the Regular Army authorized from time to time by law, and shall include the grades of chauffeur and wagoner. Chauffeurs and stable sergeants of the Medical Service Corps shall have the same rank, pay, and allowances as sergeants of the Medical Service Corps, and wagoners the same pay and allowances as wagoners of Infantry. Privates first class of the Medical Service Corps shall be eligible for ratings as surgical assistants, laboratory assistant, X-ray assistant, dispensary assistant, dental assistant, or nurse, each at \$5 a month: Provided, That no enlisted man shall receive more than

one rating for additional pay under the provisions of this section, nor shall any enlisted man receive any additional pay under such rating unless he shall have actually performed the duties for which he shall be rated.

“Except as hereinbefore provided, original appointments in the commissioned force of the Medical Service Corps shall be in the grade of first lieutenant, and first lieutenants shall, subject to the prescribed examination, be promoted to the grade of captain after five years’ service in the commissioned force of the Medical Service Corps: Provided, however, That the period during which any first lieutenant of the Medical Service Corps shall have served between April 6, 1917, and July 1, 1920, as a commissioned officer in the Army of the United States, shall be counted as a portion of the period of service required to make him eligible for promotion to the grade of captain.

“Except as hereinbefore provided, the laws governing promotion in the Medical Corps shall so far as applicable govern promotion in the commissioned force of the Medical Service Corps.

“Officers of the Medical Service Corps shall exercise command only in their own corps: Provided, That nothing in this act or any other law shall be held to deny or abridge the right of officers of the Medical Corps to exercise command in and over the Medical Service Corps.”

It is understood that Dr. Ireland also presented this plan to the general staff and received their approval and it is confidently believed therefore, that it will be embodied in the bill for Army reorganization when that is presented in Congress.

The Surgeon-General of the Navy, Dr. Braisted, has also strongly endorsed the principles embodied in the Darrow Bill, which is to provide permanent commissions for members of the Hospital Corps, up to the rank of Lieutenant Commander. A committee from the American Pharmaceutical Association and one from the National Pharmaceutical Service Association, presented this bill to Secretary Daniels in October and it is known that he has given it careful consideration and has been in conference with the Surgeon-General. The Army and Navy officials are endeavoring to coöperate in the establishment of these organizations, and the Hospital Corps of the Navy and the Medical Service Corps of the Army would practically embrace the same class of activities.

Pharmacy proper would be but one phase of the various duties

required in either organization. The filling of prescriptions and the manufacture of preparations may become a part of the duty of any member of the corps, who is properly qualified, but in addition to this, as has been explained in a number of articles appearing during the war, the members of the Hospital Corps are expected to qualify for the buying of supplies, including not only drugs, but every kind of supply for hospitals, such as food, equipment, and materials for surgical work. They are required to be first-aid men, chemists, bacteriologists, X-ray experts, stenographers, bookkeepers, commissary experts, executives, and competent aids in every department of the medical service. The question whether this work is called professional need not concern pharmacists. Much of it we know is work of which pharmacy may be proud and which does require scientific training and is properly classed as professional, but other work required by the Corps will be nonprofessional. This has been done in the past by the medical officers, who are conceded to be professional men, but the doctors did not change the work to professional work, nor can it be changed in the future. Without question, the pharmacist will be given credit for the professional work he does, as it is now conceded by the medical men of the Navy, and his standing will not be injured by the nonprofessional work required.

If both the bill proposed by Dr. Ireland and the Darrow Bill become laws, a pharmaceutical organization will be built up which will have a counterpart in the reserve corps and in these civil pharmacists will have an opportunity to enlist and receive training, and can advance as reserve officers, so that should war again occur, the reserve officers of the Hospital Corps and of the Medical Service Corps of the Army would in line for rapid promotion. It is within the jurisdiction of the Surgeon-Generals of both branches of the military service to give recognition for technical training received outside of the Army or Navy.

While it is not known just what recognition will be given graduate pharmacists in these corps, there are hundreds of cases on record in the Navy where a graduate pharmacist has advanced in eighteen months to Chief Pharmacist's Mate with the pay of about \$100 a month and all living expenses in addition. A similar opportunity will no doubt be provided in the Army and although five years of service is a requirement in the bill before commissions are granted, exceptions can be made if found practicable through a ruling of the Surgeon-Generals, as has been done in the past. It must not be



overlooked, however, that many other qualifications are necessary in addition to a technical pharmaceutical training and among these the personal qualities are important. The ability to assume command and administer an important office, becomes a prime requisite for advance.

The situation at least is encouraging and with this start, pharmacy will have every opportunity to develop in the work of the Army and the Navy during the years ahead and we believe that it can thoroughly demonstrate its importance and efficiency and that we need never again be ashamed of the place held by pharmacy in either branch of the service.

If these bills are reported favorably to Congress, ask your Congressman to give it support, and a united pharmacy at this time will be necessary to the completion of this programme and secure the recognition of pharmacy in our military organizations.

## MISCELLANEOUS MINERALOGICAL NOTES.

BY GEORGE E. ÉWE,

PHILADELPHIA, PA.

### ANALYSIS OF A POTTER'S CLAY OFFERED FOR PHARMACEUTICAL PURPOSES.

Potter's clay is a very fine, dry, smooth, grayish powder. It is employed, pharmaceutically, chiefly in the manufacture of dusting powders for use in treating chafing of the skin.

One specimen yielded the following analysis:

	Per Cent.
SiO <sub>2</sub> .....	45.25
Fe <sub>2</sub> O <sub>3</sub> .....	3.03
Al <sub>2</sub> O <sub>3</sub> .....	34.47
CaO .....	none
SO <sub>3</sub> .....	none
MgO .....	0.99
Loss upon ignition .....	11.41
Na <sub>2</sub> O + K <sub>2</sub> O (by diff.) .....	5.85
Total .....	100.00

## Analyses of 3 sericitic schists from Southern United States:

	Per Cent.
No. 1. SiO <sub>2</sub> .....	47.10
Fe <sub>2</sub> O <sub>3</sub> plus Al <sub>2</sub> O <sub>3</sub> .....	38.00
CaO .....	0.10
K <sub>2</sub> O .....	10.94
Na <sub>2</sub> O .....	3.41
H <sub>2</sub> O .....	1.65
Total .....	101.20

	Per Cent.
No. 2. SiO <sub>2</sub> .....	46.90
Fe <sub>2</sub> O <sub>3</sub> plus Al <sub>2</sub> O <sub>3</sub> .....	37.30
CaO .....	0.10
K <sub>2</sub> O .....	11.43
Na <sub>2</sub> O .....	3.81
H <sub>2</sub> O .....	0.78
Total .....	100.32

	Per Cent.
No. 3. SiO <sub>2</sub> .....	45.65
Fe <sub>2</sub> O <sub>3</sub> plus Al <sub>2</sub> O <sub>3</sub> .....	40.30
CaO .....	1.45
K <sub>2</sub> O .....	11.69
Na <sub>2</sub> O .....	3.61
H <sub>2</sub> O .....	none
Total .....	102.70

Sericitic Schist No. 3 was powdered and rendered anhydrous by gentle ignition before analysis. This schist yielded 82.9 per cent. of its total K<sub>2</sub>O by the following process:

Twice the calculated amount of sulphuric acid theoretically required to combine with the Fe<sub>2</sub>O<sub>3</sub>, Al<sub>2</sub>O<sub>3</sub>, CaO and Na<sub>2</sub>O was added to the powdered mineral and sufficient water was added to reduce the strength of the acid to approx. 30 per cent. absolute H<sub>2</sub>SO<sub>4</sub> by weight. The mixture was heated with stirring for about 8 hours on a boiling water bath, then permitted to stand at room temperature over night. This procedure rendered 44.9 per cent. of the total K<sub>2</sub>O soluble.

A second exactly similar treatment applied to the insoluble residue from the first extraction rendered still more of the total K<sub>2</sub>O soluble. The total amount of the K<sub>2</sub>O thus rendered soluble by the two extractions was 82.9 per cent. of that originally present.

ANALYSIS OF A FELDSPAR FROM VIRGINIA.—

	Per Cent.
SiO <sub>2</sub> .....	64.69
Fe <sub>2</sub> O <sub>3</sub> plus Al <sub>2</sub> O <sub>3</sub> .....	19.93
CaO .....	0.31
K <sub>2</sub> O .....	13.32
Na <sub>2</sub> O .....	2.83
H <sub>2</sub> O .....	none
Total .....	101.08

*Note.*—This mineral had been ground and rendered anhydrous by gentle ignition before assay.

EXAMINATION OF A NEPHELITE FROM MAGNET COVE, ARKANSAS.—

K <sub>2</sub> O .....	{ 3.28 } { 3.25 }	ave. 3.265 per cent.
Na <sub>2</sub> O .....	{ 9.978 } { 9.968 }	ave. 9.973 per cent.

GEYSER INCRUSTATION FROM WESTERN UNITED STATES.—This incrustation contained white patches of potassium nitrate.

SPANISH BROWN, BURNT UMBER AND BURNT SIENNA.—These are ferruginous earths, the iron being in various stages of oxidation with resultant variation in the colors of the earths. These earths are used to some extent in pharmaceutical preparations for which purpose freedom from arsenic and heavy metals, other than iron, is essential. Numerous lots of these earths were examined during the past few years and in no case were heavy metals, other than iron, found. Arsenic is frequently found, however, although not often in excessive quantities. The arsenic amounts as high as 1 part in 1,000 in some specimens. This is excessive. Only those earths in which the arsenic is present to the extent of not more than 1 part in 50,000 parts should be offered to the pharmaceutical trade and preferably the arsenic should not be greater than 1 part in 100,000 parts, which is the amount permitted in medicinal substances by the United States Pharmacopoeia.

ANALYSIS OF A TRIPOLI FROM WESTERN UNITED STATES.—This tripoli was very white, friable, and easily reducible to an excellent polishing powder.

	Per Cent.
Analysis: SiO <sub>2</sub> .....	99.14
Fe <sub>2</sub> O <sub>3</sub> + Al <sub>2</sub> O <sub>3</sub> .....	0.48
H <sub>2</sub> O .....	0.27
Total .....	99.89



FULLER'S EARTH.—This mineral is used to some extent in pharmaceutical preparations. The most objectionable impurities are heavy metals, other than iron, and arsenic.

Among the many samples examined by these laboratories during the past few years, none has been found to contain heavy metals, other than iron, and while many contained traces of arsenic, none contained this impurity in greater excess than the limit of 1 part in 100,000 parts allowed by the U. S. P. for medicinal substances.

"TERRA ALBA."—Undoubtedly this name originally was limited in its application, to white clay, but this is not now the case. During the past three or four years a white, non-setting calcium sulphate has been uniformly supplied upon orders for "Terra Alba." Previous to the past three or four years, either a white clay or a white, non-setting calcium sulphate was supplied.

For purposes of uniformity, it would be desirable for the heavy chemical trade to adopt a standard for "Terra Alba" or supply the "Terra Alba" with qualifying statements as to its chemical nature.

LABORATORIES OF H. K. MULFORD COMPANY,  
PHILADELPHIA, PA.

## THE TINCTURE OF VANILLA OF THE NATIONAL FORMULARY.<sup>1</sup>

BY BERNARD H. SMITH.

Tincture of vanilla was discontinued in the ninth edition of the Pharmacopœia, being transferred to the fourth edition of the National Formulary. The method of the eighth edition of the Pharmacopœia called for the use of 65 per cent. alcohol, which is generally recognized as being higher than is necessary to produce the best vanilla extract, but otherwise the procedure was practicable and workable. The same cannot be said of the substituted method, which is as follows:

### TINCTURE OF VANILLA.

(U. S. P. VIII.)

*Tr. Vanill.*

Vanilla, cut into small pieces, one hundred grams .....	100 Gm.
Sugar, in coarse granules, two hundred grams .....	200 Gm.
Alcohol .....	—
Diluted alcohol .....	—
Water, each a sufficient quantity .....	—
To make one thousand millimeters .....	1000 mils.

<sup>1</sup> *The Jour. of Industrial and Engr. Chem.*, Oct., 1919.

Macerate the vanilla with five hundred milliliters of alcohol in a stoppered container, in a moderately warm place, for two days with frequent agitation; then transfer it to a plain filter and reserve the filtered liquid. Spread out the drug on the filter and expose it to the air until all of the alcohol has evaporated. Then grind the vanilla and sugar to a uniform powder, pack this in a percolator and slowly percolate it with a mixture of the reserved filtrate and an equal volume of water. When the liquid ceases to drop, continue the percolation slowly, gradually adding the remainder of the prepared menstruum and then sufficient diluted alcohol to make the product measure 1,000 milliliters.

It will be noticed that the new method calls for a preliminary extraction with alcohol which contains not less than 94.9 per cent. of alcohol by volume; in other words, "Cologne spirits" of commerce. Alcohol of this strength removes a resinous extractive from the beans which is precipitated in the form of a persistent cloud when the menstruum is diluted and which is not subsequently removed by percolation or by any ordinary method of filtration. This colloidal material adds nothing to the flavor of the extract, but on the other hand renders it unsightly and unsalable.

Another obvious disadvantage of the proposed method is the loss of alcohol which its use entails. Vanilla beans of average moisture content will retain 10 per cent. of the alcohol used when placed upon a filter to drain, which is lost if the directions are followed to expose the drug "to the air until all of the alcohol has evaporated."

The method would seem to be of greater academic interest than of practical value, which is unfortunate, inasmuch as the authorities having the enforcement of the food and drug laws in charge naturally attach great importance to official methods of procedure.—Baker Extract Co., Springfield, Mass.

*Editorial Comment.*—The statements made in this paper which we reprint should not be permitted to go unchallenged. As one who, on many occasions, has employed the process of the National Formulary for the manufacture of Tincture of Vanilla, the writer is prepared to assert that this formula yields with vanilla of a satisfactory quality a product that is not only clear but that likewise complies with the standard requirements.

It is a fact well known among vanilla dealers and extract manu-

facturers that certain commercial varieties of vanilla are exceedingly difficult to manipulate and no matter what process may be used in the extraction the tincture of vanilla produced is more or less cloudy and must be clarified by subsequent manipulation. With vanilla of a satisfactory quality, the cloudy menstruum produced by diluting the reserved filtrate with an equal volume of water as directed in the N. F. formula, usually comes through as a clear percolate clarified in the process of percolation. Occasionally, it may be necessary to return the first portion of percolate until it does come through clear.

The criticism that the process as given wastes a portion of the alcohol is well founded, and doubtless every manufacturer of the tincture on a sufficient scale to justify the expense will adopt appropriate means to overcome this loss. The purpose of the formula is apparently to supply to the pharmacist, or others making the tincture on a small scale or in the quantity directed in the Formulary, a method of reducing the vanilla to the degree of fineness of powder required by the process of percolation directed. The powdering of the vanilla by itself, or in the original condition with the sugar directed, is impracticable, hence the manipulation directed. Even with this loss of alcohol, the pharmacist may be compensated by saving the manufacturér's profit and by the knowledge that he is dispensing a standard, reliable product.

The author of the paper has overlooked the fact that both the U. S. P. and N. F. establish standards for products and that each contain special notices permitting manufacturers of preparations on the large scale to deviate from the processes given provided the finished products conform to the official standards. The special notice on page XXXVIII of the N. F. Fourth Edition is intended to cover just such a condition as has occurred in the manufacture of tincture of vanilla. For the benefit of some manufacturers who may have overlooked this paragraph it is reprinted here :

*"Directions for Mixing or Manufacturing.*—Under most of the formulas are directions for manipulation to obtain the desired product. These directions have been found convenient and practicable for the quantities directed, and may apply in case of larger or smaller quantities. But such directions admit of deviations which may be more economical or convenient for manufacturing, and changes in the methods are permissible *provided the final product*



*corresponds in all respects with the one produced by the method given."*

"Deviations in the formula which result in a change in the composition of the final product are not permissible."

GEORGE M. BERINGER.

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## DEVELOPMENT OF REUNION'S VANILLA INDUSTRY (TIMES TRADE SUPPLEMENT).<sup>1</sup>

Reunion Island, a French colony a day's journey from Mauritius, and larger than the latter colony but with a small population, has suffered considerably from the war. In ordinary times its trade, which is mostly with Mauritius, Madagascar, and France, amounts to some 30,000,000 francs (say \$6,000,000) annually. Of late years this trade has been greatly reduced.

The island, all the same, holds its own as one of the greatest vanilla-producing countries in the world, and steps are being taken to improve the industry in view of the greater demands for the staple. Experts from Reunion have recently been visiting Mauritius to endeavor to secure capital for the development of their plantations, for the introduction of improved machinery on their estates, and to arrange for new, practical methods in packing their produce. As the Mauritian planters have large sums of money in hand, due to the high prices which, during the last five years, they have secured for their sugar, they have given a ready response to the appeal for capital from the Reunion colonists, and the prospects of the vanilla industry there are looking much brighter.

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## BENZINE POISONING, WITH REPORT OF A CHRONIC CASE.<sup>1</sup>

BY RUSSELL L. HADEN, M.D.,

DETROIT, MICH.

Benzine rarely causes poisoning, although it is largely used in the industrial world, especially for vulcanizing rubber, driving motors, cleaning, and as a drier in paints. Poisoning may be caused by

<sup>1</sup> From *Commerce Reports*, Oct. 10, 1919.

<sup>1</sup> Reprinted from *Johns Hopkins Hospital Bulletin*, October, 1919.

either drinking or inhaling large amounts of the substance. The absorption of small quantities seldom produces ill effects.

Benzine is a product of petroleum. It is not to be confused with benzene or benzol which is obtained by the fractional distillation of coal tar. It is not a chemically pure body, but consists of that part of petroleum which distills over between  $70^{\circ}$  and  $90^{\circ}$  C. The mixture is made up of hydrocarbons of the general formula  $C_nH_{2n+2}$ , but consists principally of hexane,  $H_6H_{14}$ , and heptane,  $C_7H_{16}$ .

Numerous experiments have been made to determine the physiologic and toxic effects of benzine. Lehman<sup>2</sup> found that the inhalation of fumes by animals caused an irritation of the respiratory mucosa, muscular twitchings, and a slowly increasing narcosis. Felix<sup>2</sup> experimented on prisoners in Bucharest, administering benzine as one would chloroform for anesthesia. Small doses produced nausea, smarting of the conjunctivæ, and, in some cases, burning in the chest and drowsiness. Larger doses caused sleep and anesthesia, succeeded by nausea, vomiting, headache, dizziness, depression, and drowsiness. Montalti,<sup>3</sup> after the internal administration of certain quantities, noted vomiting, uncomfortable feelings in the stomach, difficult breathing, miosis, muscle tremors, and symptoms of paralysis of the central nervous system. He concluded that gastrointestinal and cerebral toxic symptoms are characteristic for benzine intoxication. The action he thought to be due to the affinity of benzine for the fat, cholesterin, and lecithin group, which causes a change in the ganglion cells.

Hamilton<sup>4</sup> interviewed nine interior house-painters who had experienced the effects of using a quick-drying paint containing large quantities of benzine in small and practically unventilated rooms. Dizziness, headache, spots before the eyes, dryness with choking in the throat, and burning of the eyelids were complained of by all, while some also had nausea, vomiting, pains in various parts of the abdomen, and dysuria. In several instances the worst discomfort developed on leaving work, the dizziness and staggering coming on in the open air.

A number of cases of acute poisoning are recorded in the literature; some in children who had drunk the benzine, while others had

<sup>2</sup> Quoted by Zornlaib. *Wien. Med. Wchnschr.*, 1906, LVI, 366.

<sup>3</sup> Quoted by Hamilton.

<sup>4</sup> Hamilton, Kober and Hanson: "Diseases of Occupation and Vocational Hygiene," Philadelphia, 1916.

resulted from inhaling large amounts of the fumes, usually in cleaning tanks or vats in which there was very little ventilation. The symptoms noted as resulting from poisoning from drinking benzine have been cyanosis, miosis, weak pulse, unconsciousness, and convulsions. Friediger<sup>5</sup> has collected 14 cases of poisoning by it, eight of which resulted in death. The fatal cases were all in children. Autopsy in all cases showed hemorrhages into the lungs.

The most prominent symptom in all cases of acute poisoning from the inhalation of fumes, according to Wichern,<sup>6</sup> is the muscle tremor which may take the form of tonic or clonic cramps, the victims remaining almost without interruption in a condition of shaking fit. Wichern describes two cases: A workman was overcome by the fumes and fell into a tank of benzine. He was unconscious and showed wide, inactive pupils, spasticity, acrocyanosis, chills, and vomiting. In a second case, developing in a cleaning establishment, the symptoms were similar. Wichern states that in animal experiments muscle tremor is prominent also. Other observers have reported cases similar to those of Wichern. Peters<sup>7</sup> describes the occurrence of retrobulbar neuritis in a girl of fourteen, the daughter of a glove-cleaner, who was addicted to the habit of inhaling benzine. The child was apathetic, stubborn, and learned slowly.

Chronic benzine poisoning seems to be of rare occurrence. According to Hamilton, ordinary workmen in American oil fields and refineries show no ill effects. Russian writers state that much ill health is caused by the constant inhalation of benzine fumes in establishments where the working conditions are bad. Only four cases of chronic poisoning are to be found in the literature, all occurring in a rubber factory, and two of which are reported in detail by Dorendorf.<sup>8</sup> The first man after eight months in the factory began to have tearing pains in the muscles and joints of the extremities. Later he suffered from fibrillary twitching and a fine tremor of the hands. After a rest he went back to work. Sixteen months later he returned to the hospital complaining of pressure in the head, weak memory, difficulty in speaking, anorexia, a feeling of heaviness in the limbs, and a feeling of cold in the right hand and leg. Examination showed psychic depression, hesitant speech, weakness

<sup>5</sup> Friediger: *Münch. med. Wchnschr.*, 1912, LIX, 252.

<sup>6</sup> Wichern: *Münch. med. Wchnschr.*, 1909, LVI, 2.

<sup>7</sup> Peters: *Deut. med. Wchnschr.*, 1900, XXVI, 249.

<sup>8</sup> Dorendorf: *Münch. med. Wchnschr.*, 1901, XLVIII, 236.



of the right hand, hyperactive knee reflexes, and active tremor of the tongue, eyelids, and hand. The blood was normal except for the presence of free pigment. The second man was a worker in the vulcanizing room. A few weeks after beginning work he lost his appetite, he began to suffer from constipation, later from diarrhea, and finally from vomiting. He complained of headache and insomnia and had to stop work on account of colicky pains. He also had drawing pains in both arms and a sense of a leaden weight in the right arm with a feeling of coldness and formication. Examination showed the knee reflexes to be much increased and there was an after-tremor of the knee tendon. Striking the patella tendon evoked a contraction of the epigastric muscles and diaphragm. There was also tremor of the hands and tongue. Free pigment was found in the blood plasma, as in the first case. Dorendorf states that two other men were found in the same factory presenting similar symptoms. He allowed guinea-pigs to breathe the fumes of benzine daily and found that they developed paresis and died in convulsions in fifteen days.

The following case has been observed by us at The Johns Hopkins Hospital:

J. H. N., a white man, age forty-two, by occupation a cleaner in a lithographing factory, was admitted to the hospital October 4, 1915, complaining of weakness and dizziness.

*Family History:* His father and four brothers died of pulmonary tuberculosis, but the patient has not been associated with his family for twenty-five years.

*Previous Personal History:* The general health has been good up to two years ago. He had pneumonia at twenty-eight and malaria twice yearly for ten years. He has not had an attack of malaria for the past eight years. During the past four years he has had at times severe night sweats with cough lasting for three to four weeks. The last attack occurred two weeks before admission. He has never been jaundiced until his present illness. He had dysentery with blood and mucus in the stools in Cuba in 1897. Three years ago his appendix was removed and his right kidney suspended. For eleven years previous to this operation he had had attacks of adominal pain with a sensation of a sliding mass in the abdomen.

*Present Illness:* The patient states that he has not been strong since the operation, but in July, 1914, he felt fairly well except for some weakness. Two months after beginning his present work he

began to have generalized pains over his abdomen with nausea and vomiting after meals. He also had a feeling in his head which he describes as a "compression on the inside" or a "pressing-in like." On October 1, 1914, he went to a hospital. At this time he also had a feeling of heaviness in the arms and legs, which made them feel like leaden weights. These symptoms cleared up, but on going back to work the nausea, vomiting, and dizziness returned and have become progressively worse. The nausea and dizziness have often been so severe that he has had to leave work. He has been gradually losing strength, the weakness before admission being so extreme that it often took an hour to walk to his home when it had ordinarily required only twelve minutes. At times he has fallen in the street. For the past three months he has been getting drowsy, his memory has been failing, and he has had difficulty in thinking. He has had a feeling of coldness in his legs for the past two months, which he describes as a feeling "as if menthol were rubbed on them." He has had shooting pains in the arms with cramp in the muscles ending in hyper-extension of the fingers. Recently he has had spontaneous cramps of other muscles. His legs felt as if "a thousand needles were stuck in them." The sense of heaviness of the limbs continued until they felt like "bags of cement." He has noticed, also, tremor of the fingers and eyelids and failing memory: his head has not felt clear, and the left ear as if bubbles were flowing out of it. During all this time the nausea, vomiting, dizziness, and weakness have been progressive. He has had some dimness of vision. Five weeks before entering the hospital he noticed that his urine was becoming dark. Two days ago someone told him that he was jaundiced. He has had marked anorexia and constipation.

*Physical Examination:* The patient is undernourished and looks sick. He is very dull mentally, and answers questions slowly. There is well-marked jaundice of the skin and mucous membranes. There is a sweetish odor to the breath. The pupils are equal and active. There is no glandular enlargement. There are signs of fibroid changes at both apices. The heart is negative. Blood pressure 100/65. The liver edge extends two finger-breadths below the costal margin and is firm and tender. The spleen is palpable. The tendon reflexes are very active everywhere, but equal on the two sides. When the patella tendon on one side is struck there is a contraction of the thigh muscles on the opposite side. The super-

facial reflexes are present. Babinski and Oppenheim negative. There is no clonus; sensory examination is negative.

*Laboratory Examination:* Wassermann (blood) negative. Sputum negative for tubercle bacilli. The urine had a specific gravity of 1.022 and was negative throughout except for an occasional trace of albumin and a positive bile test on admission. Blood (October 6): R. B. C., 4,332,000; W. B. C., 4550; Hb., 77 per cent.; differential: P. M. N., 54.6 per cent.; P. M. E., 2.6 per cent.; S. M., 33.3 per cent.; L. M., 5.0 per cent.; trans., 3.0 per cent.; unclassified, 1.3 per cent. Gastric analysis: Free HCL, 44 per cent., and total acidity, 72 per cent. The stool was dark brown and gave a positive bile test. There were no parasites or ova. On October 8 the white blood cells were 5,400. A Calmette tuberculin test was negative with 1 per cent. and 5 per cent. Four other blood counts showed the white blood cells to be below 5,000. A second test meal was given with the same findings as in the first. On November 23 the white cells had risen to 7,280.

*Course in Hospital:* The symptoms rapidly disappeared. The reflexes continued active for a long while. At times striking the patella tendon would cause a contraction of nearly all the larger muscle groups. The jaundice and cyanosis cleared up. He gained weight rapidly and no longer had difficulty in thinking. He was discharged from the hospital November 23, 1915. At this time the reflexes were moderately exaggerated. Examination otherwise was negative. When seen several months later there had been no return of the symptoms.

The factory at which the patient worked was visited. It was found that the lithographing rolls were dropped into a trough, six feet long and one foot wide, filled with benzine, and scrubbed clean. About two gallons of benzine evaporated from the trough daily. The room in which the work was done was large, but from the nature of the lithographing inks it had to be tightly closed to prevent the ink from drying. The patient had worked for over a year five hours daily at this trough where he was continually inhaling the fumes. No other workmen showed signs of benzine intoxication, but there were no others engaged in the same kind of work.

Formerly each printer had been required to clean the rolls from his machine, and this took only a few minutes each day. The patient had been cleaning all the rolls for the entire factory.



# SUMMARY.

Chronic benzine poisoning is uncommon, but may occur. The symptoms complained of are referable almost entirely to the gastrointestinal tract and the central nervous system.

## FORMULAS FOR USE IN STANDARDIZING AUTOGENOUS VACCINES.<sup>1</sup>

By LEO R. TEHON, A.B.,

URBANA, ILL., SERGEANT, MEDICAL DEPARTMENT, U. S. ARMY.

In the preparation of autogenous vaccines, we used, as a routine, Wright's method of counting. In so doing I have experienced some little discomfort in handling the array of figures usually employed in making the necessary computations.

As a short cut, the formulas here given have proved useful and satisfactory, it being entirely unnecessary to compute the number of organisms per cubic centimeter in the suspension. The result obtained in working out the formulas gives the number of cubic centimeters of the suspension of organisms needed to make up a desired quantity of vaccine which will contain the desired number of organisms.

### FORMULAS.

Quantity of Vaccine.	Millions of Organisms per Cc.		
	1,000.	500.	200.
10 c.c.	$\frac{1.82 \times a}{b}$	$\frac{0.909 \times a}{b}$	$\frac{0.3636 \times a}{b}$
15 c.c.	$\frac{2.72 \times a}{b}$	$\frac{1.36 \times a}{b}$	$\frac{0.5454 \times a}{b}$
25 c.c.	$\frac{4.54 \times a}{b}$	$\frac{2.27 \times a}{b}$	$\frac{0.909 \times a}{b}$
50 c.c.	$\frac{9.09 \times a}{b}$	$\frac{4.54 \times a}{b}$	$\frac{1.818 \times a}{b}$
100 c.c.	$\frac{18.18 \times a}{b}$	$\frac{9.09 \times a}{b}$	$\frac{3.64 \times a}{b}$

In computing these formulas the number of red blood cells is arbitrarily taken to be 5.5 million per cubic millimeter; "a" is the average number of red blood cells obtained from the count, and "b" is the average number of organisms.

<sup>1</sup> From *Jour. Amer. Med. Assn.*, October 4, 1919.

Suppose we wish to make up 15 Cc. of vaccine which shall contain 500 million organisms per cubic centimeter. The red blood cell count we will suppose to have been 50, and the bacterial count 75. We now substitute these numbers in the proper formula as given, and have:

$$\frac{1.36 \times 50}{75},$$

which is equal to 0.9.

This is the number of cubic centimeters of the suspension of organisms which, when made up to 15 Cc., will give a vaccine containing 500 million organisms per cubic centimeter.

When the exact content per cubic centimeter of red blood cells is known for the blood used in the comparison, the following formula may be used in any case:

*Total number of organisms needed.*

$$\frac{b}{a} \times \text{number of r.b.c. per Cc.}$$

This gives the number of cubic centimeters of the suspension of organisms in making up a desired quantity of vaccine with a desired content of organisms.

*Note:* Hosp. Sgt. B. H. Brown, professionally an instructor in mathematics, made, at the request of the author, the first formula used by the author in standardizing vaccines. The author extends thanks and credit.

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## PRODUCTION OF CANDELILLA WAX IN MONTEREY, MEXICO.<sup>1</sup>

BY VICE CONSUL THOS. DICKINSON,  
MONTEREY.

There are great quantities of candelilla shrub in the Monterey, Mexico, consular district. It is found chiefly in the Montemorelos and Galeana districts, located in the northwestern part of the State of Nuevo Leon, also in the Bustamante and Villaldama districts, in the northern part of the State. This shrub is grown entirely with-

<sup>1</sup> From *Commerce Report*, September 12, 1919.

out cultivation. The average shrub is about 25 inches high. Some plants, however, are about 40 inches in height.

While there are several factories making candelilla wax in this consular district, there is only one large one operating at present (with a daily output of about 662 pounds of wax) due to the present low price obtaining for the product in the United States.

It is reported that another large factory in this consular district is contemplating opening shortly.

*Methods of Extracting the Wax.*—After the shrub is pulled out of the earth it is placed in wooden tanks of water which is heated to the boiling point. At the moment of boiling a certain proportion of sulphuric acid is put in the tanks. As soon as the acid comes in contact with the wax it comes to the surface and is collected and put in receptacles until it congeals; it is then put in another tank where steam is used to dissolve the wax, adding sulphuric acid a second time. The wax is then in a refined state and is allowed to harden in certain molds. It is then ready for shipment. The wax can also be extracted by direct fire.

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## THE ACTIVE PRINCIPLE OF THE THYROID GLAND.<sup>1</sup>

In our issue of March, 1919 (p. 67), reference was made to Kendall's discovery of a principle of the thyroid gland, thyro-oxy-indol or *Thyroxin*, believed to be the active principle of the gland. In a further note on the subject (*Endocrinology*, 1919, 3, 156, Apr.-June); the same author reports on its physiological action. A series of experiments by himself and others show that the action of this substance is probably that of a catalyst which bears a quantitative relation to the production of energy within the tissues. The curve representing this relation is a straight line; that is, the increase in energy production with an increasing amount of thyroxin is simply an additive one. The substance appears to function within the tissues, and there is an equilibrium between the amount in the tissues, the amount in the blood-stream, and its source of supply, the thyroid gland. The entire absence of the substance from the body does not produce death, but merely a lowering of the level at which energy can be produced by the animal organism. In administering

<sup>1</sup> From *The Prescriber*, October, 1919.



more than the normal amount of thyroxin to the animal organism there is a distinct lag in the absorption of the compound by the tissues, and there is a rapid return to the normal content if administration is stopped. The chemical reactions which are brought into play by the administration of thyroxin are probably not different from the fundamental chemical reactions occurring in its absence. As a catalyst it merely increases the rate at which these fundamental reactions are carried out. The thyroid apparatus apparently has been added to the animal organism in order to permit a greater range of flexibility of energy output.

F. Ransom (*Lancet*, 1919, 2, 433; Sept. 6) reviews the literature on the relation of iodine to the thyroid gland, referring *inter alia* to Kendall's investigations. He concludes that there is considerable probability that the active principle of the thyroid gland is a breakdown product of protein, which may be, but is not, necessarily iodized. Iodine appears to have no direct effect on the activity of the internal secretion, and yet when that activity is diminished it can often be restored by administration of iodides. This action is due to two facts: (1) iodine is specifically absorbed by the gland; (2) the iodine in the gland in saturating the unsaturated fatty acids of the blood-supply favours the autolysis by which the active principle of the gland is produced. The efficacy of iodides in tertiary syphilis may be explained on these lines, and it is anticipated that tertiary syphilis may be successfully treated with thyroid extract.

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#### CHAPARRO IN DYSENTERY: ISOLATION OF ACTIVE PRINCIPLE.<sup>1</sup>

A decoction of Chaparro amargosa (*Castela Nicholsoni*) was recommended by Nixon some years ago for amoebic dysentery (see *Prescriber*, 1914, pp. 225, 284; 1916, p. 118). Chaparro, or bitter bush, is a shrub which grows in Texas and Mexico. The entire plant is used, 6 to 8 ounces of the decoction being given by the mouth half an hour before each meal. Rectal enemata of from 500 to 2,000 Cc. are also given twice daily, these being retained as long as possible. A fluid extract is prepared, the dose of which is 60 to 180 minims. Its use has been reported in cases where emetine has failed.

<sup>1</sup> From *The Prescriber*, October, 1919.

Further experiments were reported in 1918 by Shepherd and Lillie (see *Prescriber*, May, 1918, p. 96). These investigators separated from the drug a crystalline bitter principle, but whole preparations of the drug itself gave fairly satisfactory results, those from the bitter principle were inconclusive.

Experiments were also made by Sellards and McIver, of Boston, U. S. A., who paid special attention to the chemical examination of the material (*Jour. Pharm. and Exper. Therap.*, 1918, II, 331; May). An extended analysis of the material led to the separation of a product which appears to be a glucoside or similar compound. It reduces Fehling's solution, especially after hydrolysis with hydrochloric acid. Its most characteristic chemical feature was a pronounced colour reaction with sulphuric acid. A blue colour appeared, which changed to purple, and later to brown. The substance that was separated was found to be toxic for small animals. This product has been tested among three patients suffering acute typical amoebic dysentery. The patients received one gm. of the powder three times daily at the beginning of meals. No other treatment was adopted. On the second day of treatment two of the patients improved. On the fifth day of treatment a thorough examination of the faeces failed to reveal amoebae. Some days later, purging yielded stools free from *Entamoeba histolytica*. The third patient had twice previously been "cured" by emetine, but had relapsed. Treatment with the principle obtained from chaparro produced a freedom from amoebae which has been maintained for some time.

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## THE ALLEGED FOOD VALUE OF SACCHARIN.<sup>1</sup>

Not long ago my attention was directed in the JOURNAL<sup>2</sup> to the subject of physiologic oxidation and its alleged relation to certain catalytic properities of the tissues. The latter, and particularly the blood, are capable of liberating oxygen from hydrogen peroxid by an enzyme-like reaction which has been ascribed to "catalase." It has been assumed by a few investigators, notably Burge, that a measure of this catalytic power of the tissues is an index of their metabolic activity. We need not reiterate here the criticisms of this

<sup>1</sup> From *Jour. Amer. Med. Asso.*, Nov. 8, 1919.

<sup>2</sup> "Oxidation in the Body," editorial, *J. A. M. A.*, 72: 1679 (June 7), 1919.

view which have already been advanced, notably by Becht.<sup>3</sup> He remarks that since the catalytic power of the blood varies between enormously wide limits under the same conditions, it is unlikely that the catalases are important and that the measurement of them can explain "the mysteries of the processes of oxidation." One of the factors particularly advanced by Burge in support of his theory was the asserted increase in catalase noted as the accompaniment of features known to promote metabolism. Stehle<sup>4</sup> has repeated the studies at the University of Pennsylvania School of Medicine without finding the parallelism on which the catalase theory of metabolism is based. He observed that the fluctuations in the catalase content of the blood are due to variations in the number of red cells. Consequently, Stehle notes, it is simpler to regard the catalase content as dependent on the number of erythrocytes than to assume any direct relation between catalase and biologic oxidations. Among other compounds, Burge has ascribed to saccharin the property of increasing the catalase content of the blood.<sup>5</sup> Correlating this with an increase in metabolism, he concluded that saccharin exhibits advantages characteristic of foods that are known to augment metabolism. Despite the fact that the doses used by Burge in his experiments amounted to 5 gm. per kilogram of body weight and thus far exceeded any dietetically significant quantities, his seeming approval of the effect of these enormous doses of saccharin was promptly made use of by certain advertisers to promote the use of this chemical substance in the diet. Stehle<sup>4</sup> has disposed of the assumed basis for this undesirable propaganda by what amounts essentially to a denial of the claims made. The advocacy of saccharin as a food can no longer pose in the garb of scientific proof.

<sup>3</sup> Becht, F. C.: "Observations on the Catalytic Power of Blood and Solid Tissue," *Am. J. Physiol.*, 48: 171 (March), 1919.

<sup>4</sup> Stehle, R. L.: "Some Data Concerning the Alleged Relation of Catalase for Animal Oxidations," *J. Biol. Chem.*, 39: 403 (Sept.), 1919.

<sup>5</sup> Burge, W. E.: "Saccharin for Sugar," *Science*, New York, 48: 549, 1918.



## BACTERIA AND VITAMINS.<sup>1</sup>

The demonstration that the nutritive welfare of the higher animals is dependent on an adequate supply not only of the familiar foodstuffs but also of certain as yet unidentified "food accessories," the so-called vitamins, has been stimulating in various fields of biologic science. The hypothesis of the rôle of vitamins in nutrition has been transferred to the growth of plants by Bottomley<sup>2</sup> with results that speak strongly for an analogy between plants and animals with respect to the promoting factors. Subsequently the possible part that may be played by substances analogous in function to the vitamins of animal nutrition has been debated with respect to the multiplication of bacteria.

Bacteriologists have long recognized the difficulties attending the production of cultures of microorganisms on synthetic mediums prepared from purified substances. Blood serum, tissue extracts and decoctions and other mixtures of largely unknown chemical make-up have been employed by preference as culture mediums for bacteria. For a long time the necessity of supplying such tissue products was assumed to be attributable to the fact that the lowest forms of life can attack only a limited group of fairly simple compounds. The native proteins, for example, are singularly resistant to direct disintegration by bacteria; whereas the cleavage products of proteins, the amino-acids, form an excellent nitrogenous pabulum for microbial nutrition. Latterly, however, it has become apparent that mixtures of even such simple nutrient fragments as amino-acids, sugars and inorganic salts, in mixtures of suitable reaction are poor culture mediums. To earlier evidences of the need of something more in the successful cultivation of bacteria, particularly the more delicate pathogenic varieties,<sup>3</sup> further testimony has been

<sup>1</sup> From *Jour. Amer. Med. Asso.*, Oct. 18, 1919.

<sup>2</sup> Bottomley, W. B.: "Some Accessory Factors in Plant Growth and Nutrition," *Proc. Roy. Soc. London*, Series B, 88: 237, 1914-1915.

<sup>3</sup> Cole, S. W., and Lloyd, D. J.: "The Preparation of Solid and Liquid Media for the Cultivation of the Gonococcus," *J. Path. and Bacteriol.*, 21: 267, 1916-1917. Gordon, M. H.: Hine, J. G., and Flack, M.: "An Experimental Study of the Cultural Requirements of the Meningococcus," *Brit. Med. Jour.*, 11: 678, 1916. Lloyd, D. J.: "On Vitamine, Amino-Acids and Other Chemical Factors Involved in the Growth of the Meningococcus," *J. Path. and Bactériol.*, 21: 113, 1916-1917. Agulhon, H., and Lyrroux, R.: "Contribution à l'étude des vitamines utilisables à la culture des microorganismes; application au bacille de l'influenza (B. de Pfeiffer)," *Compt. rend. Acad. d. sc.*, 167: 597, 1918.

added in the case of the diphtheria organism by Davis and Ferry<sup>4</sup> of Detroit. They found that it could not be cultivated in synthetic mediums composed of amino-acids and mineral salts adjusted to the optimal hydrogen-ion concentration. Addition of the extractives creatin and creatinin, and the purin bases xanthin and hypoxanthin, was to no advantage. Typical luxuriant growth of *Bacterium diphtheriæ* was obtained in a mixture of 99.5 per cent. of synthetic medium and only 0.5 per cent. of bouillon. Production of active toxin, however, required the presence of 10 per cent. bouillon. "Peptone" permitted only deficient growth and toxin formation. Davis and Ferry believe that such observations suggest a vitamin requirement, furnished in these cases by the beef infusion, not only for the luxuriant growth of the diphtheria bacillus but also particularly for strong toxin production. Incidentally, they believe that the results obtained favor the view that diphtheria toxin is not a synthetic product but rather "a catabolic substance elaborated by *Bacterium diphtheriæ* only in the presence of certain amino-acids and accessory factors, the latter probably of a vitamin character."

Kligler<sup>5</sup> has recently noted, in studies made at the Rockefeller Institute for Medical Research, that the growth of a large number of pathogenic bacteria, including the streptococcus, pneumococcus and meningococcus, is favorably influenced by the addition of small amounts of tissue extracts. Beef heart, rabbit and cat tissues, and human nasal secretions contain substances favorable to the growth of the organisms tested. The mucosa of different organs, spleen, liver and kidney, are relatively rich in these substances, while muscle is relatively poor. The favorable effect of the extracts is manifested by an enhancement of growth and a reduction of lag. Neither the extracts alone nor the culture medium alone was capable of supporting bacterial growth suitably. Kligler interprets his results as evidence that the facilitating substances belong to the category of the vitamins; and since ether extracts are without the potency referred to, the conclusion is further offered that the vitamins favorable for bacterial development belong to the water-soluble rather than to the fat-soluble type.

<sup>4</sup> Davis, L., and Ferry, N. S.: "Studies on Diphtheria Toxin, II, The Rôle of the Amino-Acids in the Metabolism of *Bacterium Diphtheriæ*," *J. Bacteriol.*, 4: 217 (May), 1919.

<sup>5</sup> Kligler, I. J.: "Growth Accessory Substances for Pathogenic Bacteria in Animal Tissues," *J. Exper. M.*, 30: 31 (July), 1912.

# GROWTH OF AMERICAN TRADE IN PERFUMERIES, COSMETICS, AND TOILET PREPARATIONS.<sup>1</sup>

(Prepared by the Division of Statistics, Bureau of Foreign and Domestic Commerce.)

A very substantial increase in the foreign trade of the United States in perfumeries, cosmetics, and toilet preparations occurred during the first seven months of 1919 as compared with January-July of last year, imports rising by 38 per cent., domestic exports by 110 per cent., and foreign exports (reexports) by 139 per cent. That this growth was steady month by month as compared with the corresponding figures for the previous year (with the exception of reexports in January and March) is clearly seen from the following table:

Month.	Imports.		Exports.			
			Domestic.		Foreign.	
	1918.	1919.	1918.	1919.	1918.	1919.
January.....	\$203,695	\$208,855	\$335,873	\$660,504	\$4,844	\$ 1,652
February.....	289,532	349,692	199,749	881,045	217	1,081
March.....	243,477	373,414	390,303	804,316	3,956	554
April.....	263,427	391,820	287,029	419,200	2,309	20,540
May.....	394,964	469,891	308,813	591,636	4,562	12,591
June.....	324,846	417,097	429,409	709,659	2,286	9,806
July.....	79,702	281,280	247,047	481,026	3,286	4,968
Total.....	\$1,799,643	\$2,492,049	\$2,198,223	\$4,607,386	\$21,442	\$51,195

*Fiscal Year Export Record:* The progress in this line of foreign trade is even more noticeable in the figures for fiscal years ending June 30. In 1919 imports amounted to \$3,670,577, domestic exports reached the record-breaking total of \$6,077,851, and foreign products reexported were valued at \$79,767. As compared with the corresponding figures for 1918 there is an increase of \$173,000 in imports, \$2,100,000 in exports, and \$57,000 in reexports. That this gain is no mushroom growth, nor entirely the result of war-time conditions, is evidenced by the import and export figures for the past eight fiscal years:

<sup>1</sup> From *Commerce Reports*, October 10, 1919.



Year Ended June 30.	Imports.	Exports.	
		Domestic.	Foreign.
1912 .....	\$1,645,992	\$1,147,630	\$18,652
1913 .....	1,873,585	1,441,982	9,700
1914 .....	2,309,027	1,620,872	17,969
1915 .....	2,473,144	1,715,059	11,889
1916 .....	3,105,906	2,903,063	17,682
1917 .....	3,806,699	3,618,620	12,167
1918 .....	3,497,695	3,965,465	22,724
1919 .....	3,670,577	6,077,851	79,767

Prior to the war the annual imports of perfumeries, cosmetics, and toilet preparations into the United States invariably exceeded the domestic exports. In 1912 imports surpassed the exports by nearly half a million dollars; and while every fiscal year since until 1918 has shown a material gain in the value of imports, the exports have also increased until, in 1918, they exceeded the imports by \$467,770 and in 1919 by \$2,407,274. Destination of Exports in June and July: How world-wide is the trade in American-made perfumeries, cosmetics, and toilet preparations is shown by their distribution among 77 countries in June and 66 countries in July. During these two months the Philippines were the United States' best customer, taking products of the class mentioned valued at \$155,484. China purchased to the extent of \$114,155, Canada to the extent of \$95,992, England \$73,856, Australia \$67,107, Cuba \$65,496, Denmark \$61,527, British South Africa \$58,066, Mexico \$36,983; Hongkong \$34,257, Dutch East Indies \$26,325, and South America an aggregate of \$186,153 (of which \$80,040 went to Argentina). While French, English, and German goods have had a large proportion of the Latin American trade in the past, particularly French perfumes, English fine soaps, and German articles which supplied the cheaper trade, there is now a growing demand for North American products such as talcum and face powders, creams, manicure preparations, and perfumes, if put up in attractive packages.

From a study of the export and import statistics it may be accurately inferred, notwithstanding the general rise in values, that American production has greatly increased in quantity during the last five years, in order to supply an increased domestic demand formerly dependent in considerable degree on imports chiefly from Germany, France, and Switzerland, and to take care of the foreign trade to the extent shown during the last fiscal year.

## CORRESPONDENCE.

### SPECIFICATIONS FOR CHEMICALS AND REAGENTS.

AMERICAN JOURNAL OF PHARMACY,

*Gentlemen:* The attached notes which are to be published in the *Journal of Industrial and Engineering Chemistry* for December relate to some work which is being undertaken for the benefit of analytical chemistry.

Although it is probable that nearly every chemist who would be interested in the subject will see these articles in the *Industrial Journal*, the material is being sent to a number of journals like your own which reach a certain class of readers who may have an interest in the question of specifications for chemical reagents, although they are not directly engaged in chemical work. The committee is not able to judge as to the desirability of publication or reference to this material in your journal, but is submitting it to you for any use you may desire to make of it.

Very truly yours,

W. D. COLLINS,

*Secretary,*

*Committee on Guaranteed Reagents  
and Standard Apparatus.*

### SPECIFICATIONS FOR REAGENTS.<sup>1</sup>

In the belief that a valuable service can be rendered both to the manufacturers and users of reagents and apparatus, through standardization, the American Chemical Society appointed a committee which is now organized and at present is collecting data regarding the quality of reagents on the market.

It seems that in general the experience of users agrees with that of the Bureau of Chemistry as reported by H. E. Buc in the December number of the *Journal of Industrial and Engineering Chemistry*. The chief complaints appear to be in regard to the lack of reliability of the analyses rather than unsatisfactory purity of the reagents themselves. It is also evident that in many instances impurities which have caused dissatisfaction could have been removed by exercising sufficient care in production.

<sup>1</sup> Published in the *Journal of Industrial and Engineering Chemistry*, December, 1919.

Insufficient knowledge on the part of the producer, both as to requirements and acceptable methods for testing, has been one cause for any dissatisfaction relative to reagents. Some makers have signified a willingness to follow standard specifications and methods of testing, and the committee therefore proposes to begin work on the specifications for sulphuric, nitric, and hydrochloric acids and ammonia. This will be followed with specifications for other reagents.

It is requested that suggestions be sent to the secretary of the committee, W. D. Collins, Bureau of Chemistry, Washington, indicating the specifications which would be acceptable, the uses to which the reagents are put in any special case, and the methods which are satisfactory in determining the purity of the reagents and the presence and amount of objectionable impurities.

In the near future coöperation in the standardization of laboratory apparatus will be sought.

#### CHEMICALS RECEIVED BY THE BUREAU OF CHEMISTRY DURING THE WAR.<sup>1</sup>

By H. E. Buc.

(Abstract.)

1. During the last four years about 1,300 shipments of chemicals from a large number of dealers and manufacturers have been tested in the Bureau of Chemistry. The greater part of the reagents bore an analysis on the label.

2. Most of the chemicals examined are satisfactory. Occasional impurities are found often enough in chemicals from practically all manufacturers to make it necessary to test all shipments.

3. The standard acids, ammonia, alkali salts and alkali, and most of the organic solvents are generally satisfactory.

4. The soluble salts other than alkali salts are generally acceptable but are seldom of a high degree of purity.

5. Certain organic solvents and solids are either unobtainable or unsatisfactory.

6. The insoluble products are generally unfit for use in analytical work.

<sup>1</sup> Published in *Journal of Industrial and Engineering Chemistry*, December, 1919.



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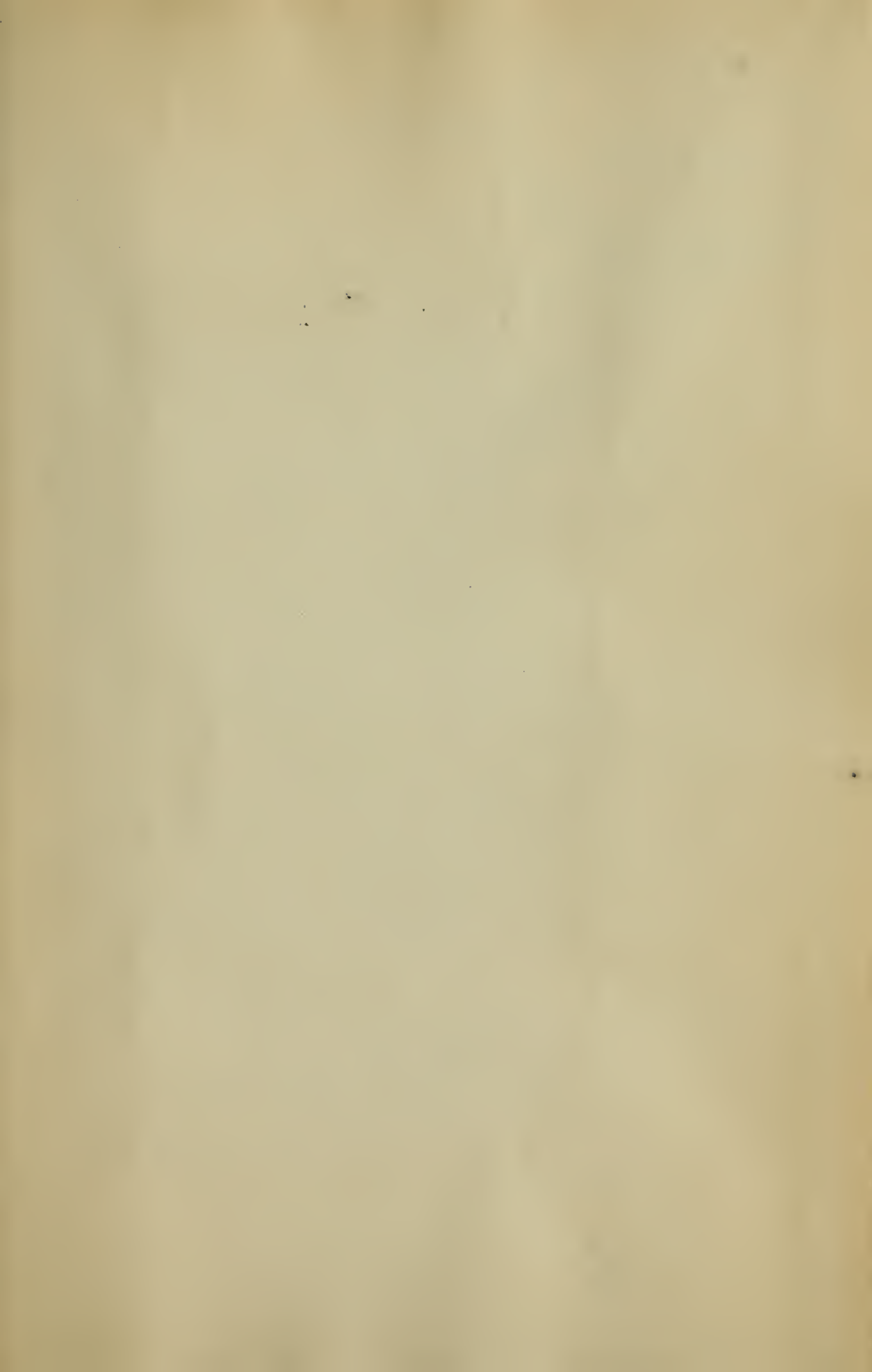
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